

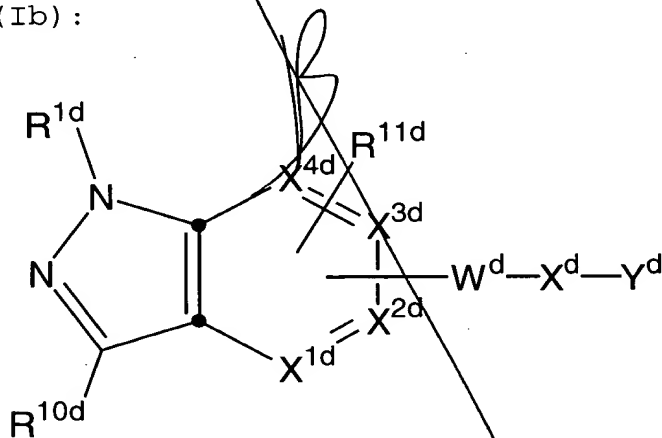
## WHAT IS CLAIMED IS DESCRIBED BELOW:

1. A compound, comprising: a targeting moiety and a  
 chelator, wherein the targeting moiety is bound to  
 the chelator, is an indazole nonpeptide, and binds  
 to a receptor that is upregulated during  
 angiogenesis and the compound has 0-1 linking groups  
 between the targeting moiety and chelator.

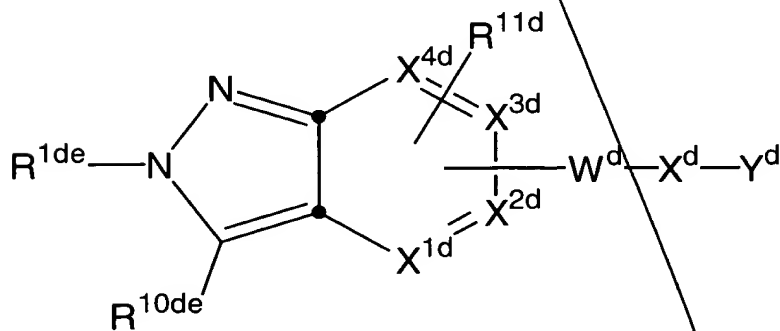
2. A compound according to Claim 1, wherein the  
 receptor is the integrin  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$  and the  
 compound is of the formula:



wherein, Q is independently a compound of Formula (Ia)  
 or (Ib):



(Ia)



(Ib)

including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof wherein:

5  $X^{1d}$  is N, CH, C- $W^d$ - $X^d$ - $Y^d$ , or C- $L_n$ ;

$X^{2d}$  is N, CH, or C- $W^d$ - $X^d$ - $Y^d$ ;

$X^{3d}$  is N, CR<sup>11d</sup>, or C- $W^d$ - $X^d$ - $Y^d$ ;

$X^{4d}$  is N or CR<sup>11d</sup>.

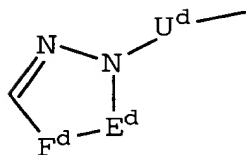
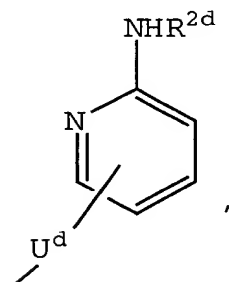
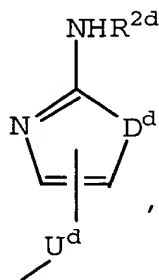
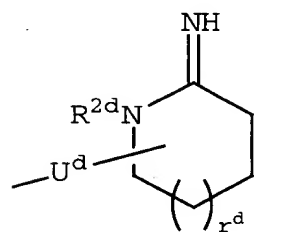
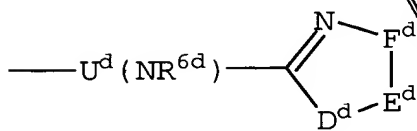
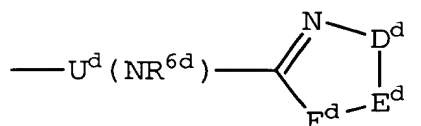
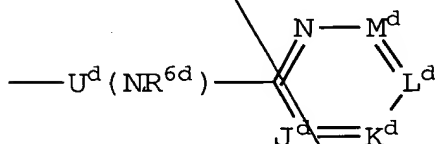
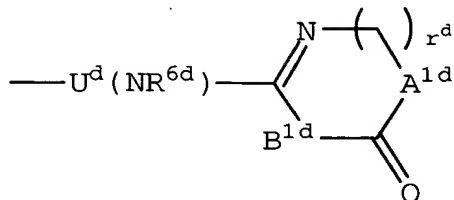
10 provided that when  $R^{1d}$  is  $R^{1de}$  then one of  $X^{1d}$  and  $X^{2d}$  is C- $W^d$ - $X^d$ - $Y^d$ , and when  $R^{10d}$  is  $R^{1de}$  then  $X^{3d}$  is C- $W^d$ - $X^d$ - $Y^d$ ;

15  $R^{1d}$  is selected from:  $R^{1de}$ , C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1  $R^{15d}$  or 0-1  $R^{21d}$ , C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1  $R^{15d}$  or 0-1  $R^{21d}$ , C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1  $R^{15d}$  or 0-1  $R^{21d}$ , C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1  $R^{15d}$  or 0-1  $R^{21d}$ , aryl substituted with 0-1  $R^{15d}$  or 0-2  $R^{11d}$  or 0-1  $R^{21d}$ , and  
20 aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1  $R^{15d}$  or 0-2  $R^{11d}$  or 0-1  $R^{21d}$ ;

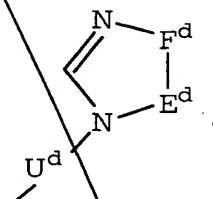
$R^{1de}$  is selected from:

or

$A^d$  and  $B^d$  are independently  $-CH_2-$ ,  $-O-$ ,  $-N(R^{2d})-$ , or



or



A<sup>d</sup> and B<sup>d</sup> are independently -CH<sub>2</sub>-, -O-, -N(R<sup>2d</sup>)-, or -C(=O)-;

A<sup>1d</sup> and B<sup>1d</sup> are independently -CH<sub>2</sub>- or -N(R<sup>3d</sup>)-;

D<sup>d</sup> is -N(R<sup>2d</sup>)-, -O-, -S-, -C(=O)- or -SO<sub>2</sub>-;

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E<sup>d</sup>-F<sup>d</sup> is -C(R<sup>4d</sup>)=C(R<sup>5d</sup>)-, -N=C(R<sup>4d</sup>)-, -C(R<sup>4d</sup>)=N-, or  
-C(R<sup>4d</sup>)<sub>2</sub>C(R<sup>5d</sup>)<sub>2</sub>-;

J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> are independently selected from

10 -C(R<sup>4d</sup>)-, -C(R<sup>5d</sup>)- and -N-, provided that at least  
one of J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> is not -N-;

R<sup>2d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, (C<sub>1</sub>-C<sub>6</sub>  
alkyl)carbonyl, (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl; (C<sub>1</sub>-C<sub>6</sub>  
15 alkyl)aminocarbonyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
alkyl)carbonyl, heteroarylcabonyl,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl-,  
arylcabonyl, C<sub>1</sub>-C<sub>6</sub> alkylsulfonyl, arylsulfonyl,  
20 aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)sulfonyl, heteroarylsulfonyl,  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)sulfonyl, aryloxycarbonyl, and  
aryl(C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl, wherein said aryl groups  
are substituted with 0-2 substituents selected from  
the group: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, CF<sub>3</sub>, and  
25 nitro;

R<sup>3d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

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R<sup>4d</sup> and R<sup>5d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>4</sub>  
alkoxy, NR<sup>2d</sup>R<sup>3d</sup>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl,  
C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, (C<sub>1</sub>-C<sub>6</sub>

alkyl)carbonyl, (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl, and  
arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R<sup>4d</sup>

5 and R<sup>5d</sup> can be taken together with the carbon atoms  
to which they are attached to form a 5-7 membered  
carbocyclic or 5-7 membered heterocyclic aromatic or  
non-aromatic ring system, said carbocyclic or  
heterocyclic ring being optionally substituted with  
10 0-2 groups selected from: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy,  
halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

U<sup>d</sup> is selected from:

- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>-,
- 15 - (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(CR<sup>7d</sup>=CR<sup>8d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C≡C)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>t<sup>d</sup></sub>Q(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>O(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- 20 - (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>C(=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C=O)N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(C=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-, and
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>S(O)<sub>p<sup>d</sup></sub>(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-;

wherein one or more of the methylene groups in U<sup>d</sup> is

25 optionally substituted with R<sup>7d</sup>;

Q<sup>d</sup> is selected from 1,2-cycloalkylene, 1,2-phenylene,  
1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-  
pyridinylene, 2,4-pyridinylene, and 3,4-  
30 pyridazinylene;

R<sup>6d</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkyl, and benzyl;

R<sup>7d</sup> and R<sup>8d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and heteroaryl(C<sub>0</sub>-C<sub>6</sub> alkyl)-;

R<sup>10d</sup> is selected from: H, R<sup>1de</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

R<sup>10de</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

R<sup>11d</sup> is selected from H, halogen, CF<sub>3</sub>, CN, NO<sub>2</sub>, hydroxy, NR<sup>2d</sup>R<sup>3d</sup>, C<sub>1</sub>-C<sub>4</sub> alkyl substituted with 0-1 R<sup>21d</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>21d</sup>, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>21d</sup>, (C<sub>1</sub>-C<sub>4</sub> alkoxy)carbonyl substituted with 0-1 R<sup>21d</sup>, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl substituted with 0-1 R<sup>21d</sup>,

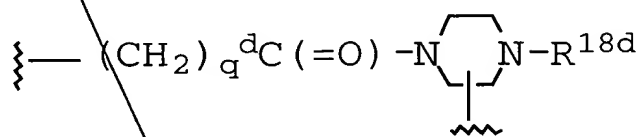
C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl substituted with 0-1 R<sup>21d</sup>, and  
C<sub>1</sub>-C<sub>4</sub> alkylaminosulfonyl substituted with 0-1 R<sup>21d</sup>;

W<sup>d</sup> is selected from:

- 5    -(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>C(=O)N(R<sup>13d</sup>)-, and  
     -C(=O)-N(R<sup>13d</sup>)-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>-;

X<sup>d</sup> is -C(R<sup>12d</sup>)(R<sup>14d</sup>)-C(R<sup>12d</sup>)(R<sup>15d</sup>)-; or  
alternatively, W<sup>d</sup> and X<sup>d</sup> can be taken together to be

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R<sup>12d</sup> is selected from H, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub>  
alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
15    C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl, aryl,  
and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>13d</sup> is selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub>  
cycloalkylmethyl, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

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R<sup>14d</sup> is selected from:

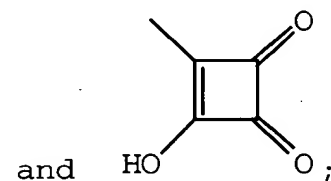
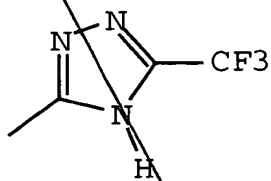
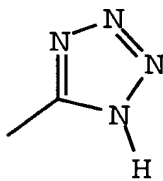
- H, C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub>  
alkylthioalkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl)-, C<sub>1</sub>-C<sub>10</sub>  
alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>2</sub>-C<sub>10</sub>  
25    alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-C<sub>10</sub>  
cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
alkyl)-, aryl, heteroaryl, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, and  
CONR<sup>17d</sup>R<sup>20d</sup>, provided that any of the above alkyl,  
cycloalkyl, aryl or heteroaryl groups may be  
30    unsubstituted or substituted independently with 0-1  
R<sup>16d</sup> or 0-2 R<sup>11d</sup>;

R<sup>15d</sup> is selected from:

H, R<sup>16d</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl,  
 C<sub>1</sub>-C<sub>10</sub> alkylaminoalkyl, C<sub>1</sub>-C<sub>10</sub> dialkylaminoalkyl,  
 (C<sub>1</sub>-C<sub>10</sub> alkyl)carbonyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl,  
 5 C<sub>1</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-  
 C<sub>10</sub> cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-,  
 heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl, heteroaryl, CO<sub>2</sub>R<sup>17d</sup>,  
 C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, SO<sub>2</sub>R<sup>17d</sup>, and SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>,  
 provided that any of the above alkyl, cycloalkyl,  
 10 aryl or heteroaryl groups may be unsubstituted or  
 substituted independently with 0-2 R<sup>11d</sup>;

Y<sup>d</sup> is selected from:

-COR<sup>19d</sup>, -SO<sub>3</sub>H, -PO<sub>3</sub>H, tetrazolyl, -CONHNHSO<sub>2</sub>CF<sub>3</sub>, -  
 15 CONHSO<sub>2</sub>R<sup>17d</sup>, -CONHSO<sub>2</sub>NHR<sup>17d</sup>, -NHCOCF<sub>3</sub>, -NHCONHSO<sub>2</sub>R<sup>17d</sup>,  
 -NHSO<sub>2</sub>R<sup>17d</sup>, -OPO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H, -PO<sub>3</sub>H<sub>2</sub>, -SO<sub>3</sub>H, -  
 SO<sub>2</sub>NHCOR<sup>17d</sup>, -SO<sub>2</sub>NHCO<sub>2</sub>R<sup>17d</sup>,



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R<sup>16d</sup> is selected from:

-N(R<sup>20d</sup>)-C(=O)-O-R<sup>17d</sup>,  
 -N(R<sup>20d</sup>)-C(=O)-R<sup>17d</sup>,  
 -N(R<sup>20d</sup>)-C(=O)-NH-R<sup>17d</sup>,  
 25 -N(R<sup>20d</sup>)SO<sub>2</sub>-R<sup>17d</sup>, and  
 -N(R<sup>20d</sup>)SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

R<sup>17d</sup> is selected from:

C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with a bond to  
 30 L<sub>n</sub>, C<sub>3</sub>-C<sub>11</sub> cycloalkyl optionally substituted with a  
 bond to L<sub>n</sub>, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally substituted



with a bond to  $L_n$ , ( $C_1$ - $C_6$  alkyl)aryl optionally substituted with a bond to  $L_n$ , heteroaryl( $C_1$ - $C_6$  alkyl)- optionally substituted with a bond to  $L_n$ , ( $C_1$ - $C_6$  alkyl)heteroaryl optionally substituted with a bond to  $L_n$ , biaryl( $C_1$ - $C_6$  alkyl)- optionally substituted with a bond to  $L_n$ , heteroaryl optionally substituted with a bond to  $L_n$ , aryl optionally substituted with a bond to  $L_n$ , biaryl optionally substituted with a bond to  $L_n$ , and a bond to  $L_n$ , wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of:  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  alkoxy, aryl, heteroaryl, halo, cyano, amino,  $CF_3$ , and  $NO_2$ ;

$R^{18d}$  is selected from:

-H,  
 $-C(=O)-O-R^{17d}$ ,  
 $-C(=O)-R^{17d}$ ,  
 $-C(=O)-NH-R^{17d}$ ,  
 $-SO_2-R^{17d}$ , and  
 $-SO_2-NR^{20d}R^{17d}$ ;

$R^{19d}$  is selected from: hydroxy,  $C_1$ - $C_{10}$  alkyloxy,  $C_3$ - $C_{11}$  cycloalkyloxy, aryloxy, aryl( $C_1$ - $C_6$  alkoxy)-,  $C_3$ - $C_{10}$  alkylcarbonyloxyalkyloxy,  $C_3$ - $C_{10}$  alkoxy carbonyloxyalkyloxy,  $C_2$ - $C_{10}$  alkoxy carbonylalkyloxy,  $C_5$ - $C_{10}$  cycloalkylcarbonyloxyalkyloxy,  $C_5$ - $C_{10}$  cycloalkoxy carbonyloxyalkyloxy,  $C_5$ - $C_{10}$  cycloalkoxy carbonylalkyloxy,  $C_7$ - $C_{11}$  aryloxy carbonylalkyloxy,  $C_8$ - $C_{12}$  aryloxy carbonyloxyalkyloxy,  $C_8$ - $C_{12}$  arylcarbonyloxyalkyloxy,

C<sub>5</sub>-C<sub>10</sub> alkoxyalkylcarbonyloxyalkyloxy,  
 C<sub>5</sub>-C<sub>10</sub> (5-alkyl-1,3-dioxo-cyclopenten-2-one-  
 yl)methyloxy, C<sub>10</sub>-C<sub>14</sub> (5-aryl-1,3-dioxo-cyclopenten-  
 2-one-yl)methyloxy, and  
 5 (R<sup>11d</sup>) (R<sup>12d</sup>)N-(C<sub>1</sub>-C<sub>10</sub> alkoxy)-;

R<sup>20d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
 C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
 heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

10 R<sup>21d</sup> is selected from: COOH and NR<sup>6d</sup><sub>2</sub>;

m<sup>d</sup> is 0-4;

n<sup>d</sup> is 0-4;

t<sup>d</sup> is 0-4;

15 p<sup>d</sup> is 0-2;

q<sup>d</sup> is 0-2; and

r<sup>d</sup> is 0-2;

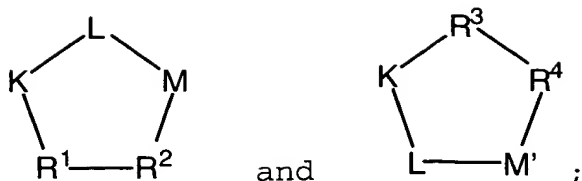
with the following provisos:

20 (1) t<sup>d</sup>, n<sup>d</sup>, m<sup>d</sup> and q<sup>d</sup> are chosen such that the number of  
 atoms connecting R<sup>1d</sup> and Y<sup>d</sup> is in the range of 10-14;  
 and

(2) n<sup>d</sup> and m<sup>d</sup> are chosen such that the value of n<sup>d</sup> plus  
 m<sup>d</sup> is greater than one unless U<sup>d</sup> is

25  $-(\text{CH}_2)_t \text{Q}^{\text{d}} (\text{CH}_2)_m^-$ ;

or Q is a peptide selected from the group:



R<sup>1</sup> is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L<sub>n</sub>;

5

R<sup>2</sup> is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L<sub>n</sub>;

10

R<sup>3</sup> is D-valine;

R<sup>4</sup> is D-tyrosine substituted on the hydroxy group with a bond to L<sub>n</sub>;

15

provided that one of R<sup>1</sup> and R<sup>2</sup> in each Q is substituted with a bond to L<sub>n</sub>, and further provided that when R<sup>2</sup> is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

20

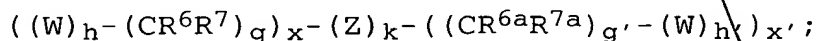
provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25

d' is 1-100;

L<sub>n</sub> is a linking group having the formula:



30

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, NR<sup>8</sup>C(=O), C(=O)N

$R^8$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $NHC(=S)NH$ ,  $NHC(=O)NH$ ,  $SO_2$ ,  
 $SO_2NH$ ,  $(OCH_2CH_2)_s$ ,  $(CH_2CH_2O)_s$ ,  $(OCH_2CH_2CH_2)_s$ ,  
 $(CH_2CH_2CH_2O)_t$ , and  $(aa)_t$ ;

5 aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3  
 $R^{10}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-3  $R^{10}$ , and a  
 5-10 membered heterocyclic ring system containing  
 10 1-4 heteroatoms independently selected from N, S,  
 and O and substituted with 0-3  $R^{10}$ ;

$R^6$ ,  $R^{6a}$ ,  $R^7$ ,  $R^{7a}$ , and  $R^8$  are independently selected at  
 each occurrence from the group: H, =O, COOH,  $SO_3H$ ,  
 15  $PO_3H$ ,  $C_1-C_5$  alkyl substituted with 0-3  $R^{10}$ , aryl  
 substituted with 0-3  $R^{10}$ , benzyl substituted with 0-3  
 $R^{10}$ , and  $C_1-C_5$  alkoxy substituted with 0-3  $R^{10}$ ,  
 $NHC(=O)R^{11}$ ,  $C(=O)NHR^{11}$ ,  $NHC(=O)NHR^{11}$ ,  $NHR^{11}$ ,  $R^{11}$ , and  
 a bond to  $Ch$ ;

20  $R^{10}$  is independently selected at each occurrence from the  
 group: a bond to  $Ch$ ,  $COOR^{11}$ ,  $C(=O)NHR^{11}$ ,  $NHC(=O)R^{11}$ ,  
 $OH$ ,  $NHR^{11}$ ,  $SO_3H$ ,  $PO_3H$ ,  $-OPO_3H_2$ ,  $-OSO_3H$ , aryl  
 substituted with 0-3  $R^{11}$ ,  $C_{1-5}$  alkyl substituted with  
 25 0-1  $R^{12}$ ,  $C_{1-5}$  alkoxy substituted with 0-1  $R^{12}$ , and a  
 5-10 membered heterocyclic ring system containing  
 1-4 heteroatoms independently selected from N, S,  
 and O and substituted with 0-3  $R^{11}$ ;

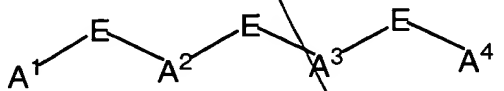
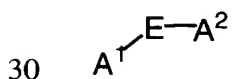
30  $R^{11}$  is independently selected at each occurrence from the  
 group: H, alkyl substituted with 0-1  $R^{12}$ , aryl  
 substituted with 0-1  $R^{12}$ , a 5-10 membered  
 heterocyclic ring system containing 1-4 heteroatoms  
 independently selected from N, S, and O and

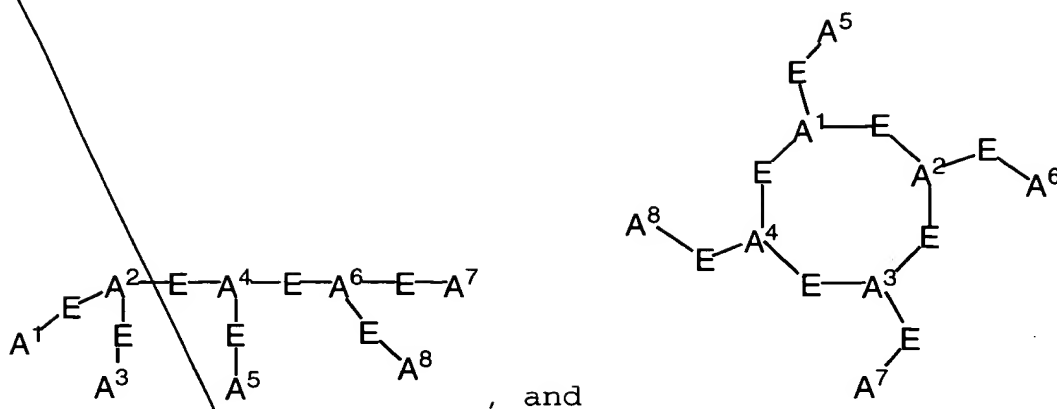
substituted with 0-1  $R^{12}$ ,  $C_{3-10}$  cycloalkyl  
 substituted with 0-1  $R^{12}$ , polyalkylene glycol  
 substituted with 0-1  $R^{12}$ , carbohydrate substituted  
 with 0-1  $R^{12}$ , cyclodextrin substituted with 0-1  $R^{12}$ ,  
 5 amino acid substituted with 0-1  $R^{12}$ , polycarboxyalkyl  
 substituted with 0-1  $R^{12}$ , polyazaalkyl substituted  
 with 0-1  $R^{12}$ , and peptide substituted with 0-1  $R^{12}$ ,  
 wherein the peptide is comprised of 2-10 amino  
 acids, 3,6-O-disulfo-B-D-galactopyranosyl,  
 10 bis(phosphonomethyl)glycine, and a bond to  $C_h$ ;

$R^{12}$  is a bond to  $C_h$ ;

k is selected from 0, 1, and 2;  
 15 h is selected from 0, 1, and 2;  
 h' is selected from 0, 1, and 2;  
 g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 20 s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;  
 x is selected from 0, 1, 2, 3, 4, and 5;  
 25 x' is selected from 0, 1, 2, 3, 4, and 5;

$C_h$  is a metal bonding unit having a formula selected from  
 the group:





A<sup>1</sup>, A<sup>2</sup>, A<sup>3</sup>, A<sup>4</sup>, A<sup>5</sup>, A<sup>6</sup>, A<sup>7</sup>, and A<sup>8</sup> are independently selected at each occurrence from the group: NR<sup>13</sup>,  
 5 NR<sup>13</sup>R<sup>14</sup>, S, SH, S(Pg), O, OH, PR<sup>13</sup>, PR<sup>13</sup>R<sup>14</sup>, P(O)R<sup>15</sup>R<sup>16</sup>, and a bond to L<sub>n</sub>;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>,  
 10 C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, heterocyclo-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C<sub>6-10</sub>  
 15 aryl-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub> alkyl-C<sub>6-10</sub> aryl- substituted with 0-3 R<sup>17</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

R<sup>13</sup> and R<sup>14</sup> are each independently selected from the group: a bond to L<sub>n</sub>, hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>,  
 25 R<sup>17</sup>, C<sub>1-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, heterocyclo-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>,

wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C<sub>6-10</sub> aryl-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub> alkyl-C<sub>6-10</sub> aryl- substituted with 0-3 R<sup>17</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>, and an electron, provided that when one of R<sup>13</sup> or R<sup>14</sup> is an electron, then the other is also an electron;

alternatively, R<sup>13</sup> and R<sup>14</sup> combine to form =C(R<sup>20</sup>)(R<sup>21</sup>);

R<sup>15</sup> and R<sup>16</sup> are each independently selected from the group: a bond to L<sub>n</sub>, -OH, C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, heterocyclo-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C<sub>6-10</sub> aryl-C<sub>1-10</sub> alkyl substituted with 0-3 R<sup>17</sup>, C<sub>1-10</sub> alkyl-C<sub>6-10</sub> aryl- substituted with 0-3 R<sup>17</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

R<sup>17</sup> is independently selected at each occurrence from the group: a bond to L<sub>n</sub>, =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CHO, -CH<sub>2</sub>OR<sup>18</sup>, -OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OR<sup>18</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>C(=O)R<sup>18</sup>, -NR<sup>19</sup>C(=O)OR<sup>18a</sup>, -NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>,

$-\text{NR}^{19}\text{SO}_2\text{N}(\text{R}^{18})_2$ ,  $-\text{NR}^{19}\text{SO}_2\text{R}^{18a}$ ,  $-\text{SO}_3\text{H}$ ,  $-\text{SO}_2\text{R}^{18a}$ ,  
 $-\text{SR}^{18}$ ,  $-\text{S}(=\text{O})\text{R}^{18a}$ ,  $-\text{SO}_2\text{N}(\text{R}^{18})_2$ ,  $-\text{N}(\text{R}^{18})_2$ ,  
 $-\text{NHC}(=\text{S})\text{NHR}^{18}$ ,  $=\text{NOR}^{18}$ ,  $\text{NO}_2$ ,  $-\text{C}(=\text{O})\text{NHOR}^{18}$ ,  
 $-\text{C}(=\text{O})\text{NHN}(\text{R}^{18})_2$ ,  $-\text{OCH}_2\text{CO}_2\text{H}$ , 2-(1-morpholino)ethoxy,  
 5 C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub>  
 cycloalkylmethyl, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl, aryl  
 substituted with 0-2 R<sup>18</sup>, and a 5-10 membered  
 heterocyclic ring system containing 1-4 heteroatoms  
 independently selected from N, S, and O;

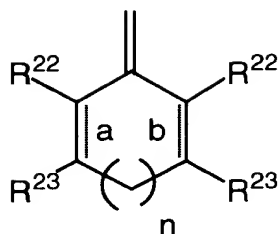
10 R<sup>18</sup>, R<sup>18a</sup>, and R<sup>19</sup> are independently selected at each  
 occurrence from the group: a bond to L<sub>n</sub>, H, C<sub>1</sub>-C<sub>6</sub>  
 alkyl, phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halide, nitro,  
 cyano, and trifluoromethyl;

15 Pg is a thiol protecting group;

20 R<sup>20</sup> and R<sup>21</sup> are independently selected from the group: H,  
 C<sub>1</sub>-C<sub>10</sub> alkyl,  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^{25}$ ,  $-\text{C}(=\text{O})\text{R}^{25}$ ,  $-\text{C}(=\text{O})\text{N}(\text{R}^{25})_2$ ,  
 C<sub>2</sub>-C<sub>10</sub> 1-alkene substituted with 0-3 R<sup>23</sup>, C<sub>2</sub>-C<sub>10</sub>  
 1-alkyne substituted with 0-3 R<sup>23</sup>, aryl substituted  
 with 0-3 R<sup>23</sup>, unsaturated 5-10 membered heterocyclic  
 ring system containing 1-4 heteroatoms independently  
 selected from N, S, and O and substituted with 0-3  
 25 R<sup>23</sup>, and unsaturated C<sub>3</sub>-<sub>10</sub> carbocycle substituted  
 with 0-3 R<sup>23</sup>;

alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the  
 divalent carbon radical to which they are attached  
 30 form:





$R^{22}$  and  $R^{23}$  are independently selected from the group: H,  
 $R^{24}$ , C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3  $R^{24}$ , C<sub>2</sub>-C<sub>10</sub>  
 5 alkenyl substituted with 0-3  $R^{24}$ , C<sub>2</sub>-C<sub>10</sub> alkynyl  
 substituted with 0-3  $R^{24}$ , aryl substituted with 0-3  
 $R^{24}$ , a 5-10 membered heterocyclic ring system  
 containing 1-4 heteroatoms independently selected  
 from N, S, and O and substituted with 0-3  $R^{24}$ , and  
 10 C<sub>3</sub>-10 carbocycle substituted with 0-3  $R^{24}$ ;

alternatively,  $R^{22}$ ,  $R^{23}$  taken together form a fused  
 aromatic or a 5-10 membered heterocyclic ring system  
 containing 1-4 heteroatoms independently selected  
 15 from N, S, and O;

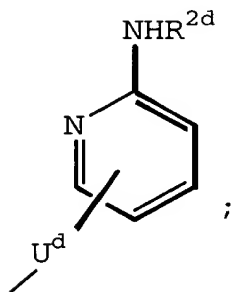
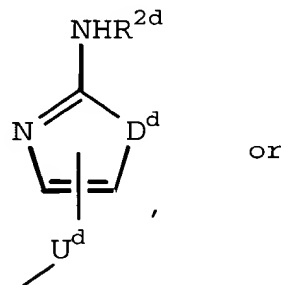
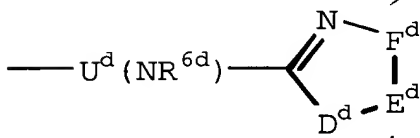
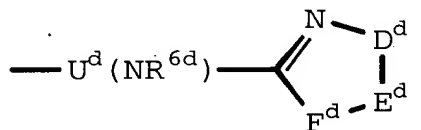
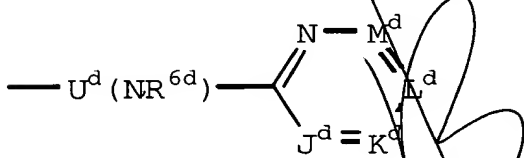
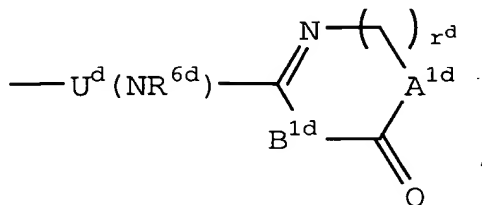
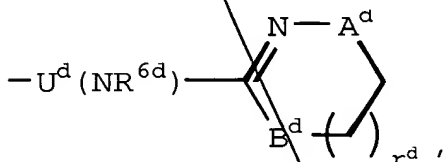
a and b indicate the positions of optional double bonds  
 and n is 0 or 1;

20  $R^{24}$  is independently selected at each occurrence from the  
 group: =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub>R<sup>25</sup>,  
 -C(=O)R<sup>25</sup>, -C(=O)N(R<sup>25</sup>)<sub>2</sub>, -N(R<sup>25</sup>)<sub>3</sub><sup>+</sup>, -CH<sub>2</sub>OR<sup>25</sup>,  
 -OC(=O)R<sup>25</sup>, -OC(=O)OR<sup>25a</sup>, -OR<sup>25</sup>, -OC(=O)N(R<sup>25</sup>)<sub>2</sub>,  
 -NR<sup>26</sup>C(=O)R<sup>25</sup>, -NR<sup>26</sup>C(=O)OR<sup>25a</sup>, -NR<sup>26</sup>C(=O)N(R<sup>25</sup>)<sub>2</sub>,  
 25 -NR<sup>26</sup>SO<sub>2</sub>N(R<sup>25</sup>)<sub>2</sub>, -NR<sup>26</sup>SO<sub>2</sub>R<sup>25a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>25a</sup>, -SR<sup>25</sup>,  
 -S(=O)R<sup>25a</sup>, -SO<sub>2</sub>N(R<sup>25</sup>)<sub>2</sub>, -N(R<sup>25</sup>)<sub>2</sub>, =NOR<sup>25</sup>,  
 -C(=O)NHOR<sup>25</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H, and 2-(1-morpholino)ethoxy;  
 and,

R<sup>25</sup>, R<sup>25a</sup>, and R<sup>26</sup> are each independently selected at each occurrence from the group: hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl.

5 3. A compound according to Claim 2, wherein:

$R^{1de}$  is selected from:



10

A<sup>d</sup> and B<sup>d</sup> are independently -CH<sub>2</sub>-, -O-, -N(R<sup>2d</sup>)-, or -C(=O)-;

$A^{1d}$  and  $B^{1d}$  are independently  $-CH_2-$  or  $-N(R^{3d})-$ ;

$D^d$  is  $-N(R^{2d})-$ ,  $-O-$ ,  $-S-$ ,  $-C(=O)-$  or  $-SO_2-$ ;

5  $E^d-F^d$  is  $-C(R^{4d})=C(R^{5d})-$ ,  $-N=C(R^{4d})-$ ,  $-C(R^{4d})=N-$ , or  $-C(R^{4d})_2C(R^{5d})_2-$ ;

$J^d$ ,  $K^d$ ,  $L^d$  and  $M^d$  are independently selected from:  
 $C(R^{4d})-$ ,  $-C(R^{5d})-$  and  $-N-$ , provided that at least one  
 10 of  $J^d$ ,  $K^d$ ,  $L^d$  and  $M^d$  is not  $-N-$ ;

$R^{2d}$  is selected from: H,  $C_1-C_6$  alkyl,  $(C_1-C_6$   
 alkyl)carbonyl,  $(C_1-C_6$  alkoxy)carbonyl,  $C_1-C_6$   
 alkylaminocarbonyl,  $C_3-C_6$  alkenyl,  $C_3-C_7$  cycloalkyl,  
 15  $C_4-C_{11}$  cycloalkylalkyl, aryl, heteroaryl( $C_1-C_6$   
 alkyl)carbonyl, heteroarylcarbonyl, aryl( $C_1-C_6$   
 alkyl)-,  $(C_1-C_6$  alkyl)carbonyl, arylcarbonyl,  
 alkylsulfonyl, arylsulfonyl, aryl( $C_1-C_6$   
 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl( $C_1-C_6$   
 20 alkyl)sulfonyl, aryloxy carbonyl, and aryl( $C_1-C_6$   
 alkoxy)carbonyl, wherein said aryl groups are  
 substituted with 0-2 substituents selected from the  
 group consisting of  $C_1-C_4$  alkyl,  $C_1-C_4$  alkoxy, halo,  
 $CF_3$ , and nitro;

25  $R^{3d}$  is selected from: H,  $C_1-C_6$  alkyl,  $C_3-C_7$  cycloalkyl,  
 $C_4-C_{11}$  cycloalkylalkyl, aryl, aryl( $C_1-C_6$  alkyl)-, and  
 heteroaryl( $C_1-C_6$  alkyl)-;

30  $R^{4d}$  and  $R^{5d}$  are independently selected from: H,  $C_1-C_4$   
 alkoxy,  $NR^{2d}R^{3d}$ , halogen,  $NO_2$ , CN,  $CF_3$ ,  $C_1-C_6$  alkyl,  
 $C_3-C_6$  alkenyl,  $C_3-C_7$  cycloalkyl,  $C_4-C_{11}$

cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, C<sub>2</sub>-C<sub>7</sub> alkylcarbonyl, and arylcarbonyl;

alternatively, when substituents on adjacent atoms, R<sup>4d</sup>

5 and R<sup>5d</sup> can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with  
10 0-2 groups selected from: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, cyano, amino, CF<sub>3</sub>, or NO<sub>2</sub>;

U<sup>d</sup> is selected from:

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> (CR<sup>7d</sup>=CR<sup>8d</sup>) (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

15 -(CH<sub>2</sub>)<sub>t</sub><sup>d</sup> Q<sup>d</sup> (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> O(CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> N(R<sup>6d</sup>) (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> C(=O) (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-, and

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> S(O)<sub>p</sub><sup>d</sup> (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-;

20

wherein one or more of the methylene groups in U<sup>d</sup> is optionally substituted with R<sup>7d</sup>;

Q<sup>d</sup> is selected from 1,2-phenylene, 1,3-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, and 2,4-pyridinylene;

25

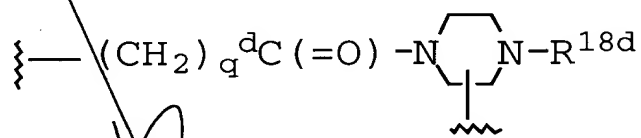
R<sup>6d</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkyl, and benzyl;

$R^{7d}$  and  $R^{8d}$  are independently selected from: H,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_7$  cycloalkyl,  $C_4$ - $C_{11}$  cycloalkylalkyl, aryl, aryl( $C_1$ - $C_6$  alkyl)-, and heteroaryl( $C_0$ - $C_6$  alkyl)-;

$W^d$  is  $-C(=O)-N(R^{13d})-(C(R^{12d})_2)_q^d-$ ;

$X^d$  is  $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$ ;

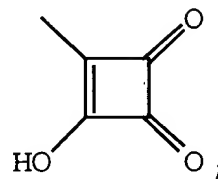
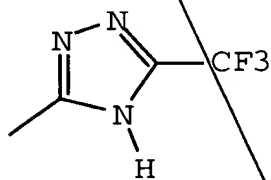
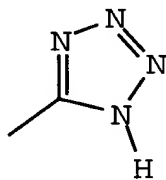
alternatively,  $W^d$  and  $X^d$  can be taken together to be



$R^{12d}$  is H or  $C_1$ - $C_6$  alkyl;

$Y^d$  is selected from:

$-\text{COR}^{19d}$ ,  $-\text{SO}_3\text{H}$ ,



$d$  is selected from 1, 2, 3, 4, and 5;

$d'$  is 1-50;

$W$  is independently selected at each occurrence from the group: O, NH,  $\text{NHC}(=\text{O})$ ,  $\text{C}(=\text{O})\text{NH}$ ,  $\text{NR}^8\text{C}(=\text{O})$ ,  $\text{C}(=\text{O})\text{NR}^8$ ,  $\text{C}(=\text{O})$ ,  $\text{C}(=\text{O})\text{O}$ ,  $\text{OC}(=\text{O})$ ,  $\text{NHC}(=\text{S})\text{NH}$ ,  $\text{NHC}(=\text{O})\text{NH}$ ,  $\text{SO}_2$ ,

$(\text{OCH}_2\text{CH}_2)_s$ ,  $(\text{CH}_2\text{CH}_2\text{O})_{s'}$ ,  $(\text{OCH}_2\text{CH}_2\text{CH}_2)_{s''}$ ,  $(\text{CH}_2\text{CH}_2\text{CH}_2\text{O})_t$ ,  
and  $(\text{aa})_t$ ;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1  $\text{R}^{10}$ ,  $\text{C}_3\text{-10}$  cycloalkyl substituted with 0-1  $\text{R}^{10}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1  $\text{R}^{10}$ ;

$\text{R}^6$ ,  $\text{R}^{6a}$ ,  $\text{R}^7$ ,  $\text{R}^{7a}$ , and  $\text{R}^8$  are independently selected at each occurrence from the group: H, =O,  $\text{COOH}$ ,  $\text{SO}_3\text{H}$ ,  $\text{C}_1\text{-C}_5$  alkyl substituted with 0-1  $\text{R}^{10}$ , aryl substituted with 0-1  $\text{R}^{10}$ , benzyl substituted with 0-1  $\text{R}^{10}$ , and  $\text{C}_1\text{-C}_5$  alkoxy substituted with 0-1  $\text{R}^{10}$ ,  $\text{NHC}(=\text{O})\text{R}^{11}$ ,  $\text{C}(=\text{O})\text{NHR}^{11}$ ,  $\text{NHC}(=\text{O})\text{NHR}^{11}$ ,  $\text{NHR}^{11}$ ,  $\text{R}^{11}$ , and a bond to  $\text{C}_h$ ;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s'' is selected from 0, 1, 2, 3, 4, and 5;

t is selected from 0, 1, 2, 3, 4, and 5;

$\text{A}^1$ ,  $\text{A}^2$ ,  $\text{A}^3$ ,  $\text{A}^4$ ,  $\text{A}^5$ ,  $\text{A}^6$ ,  $\text{A}^7$ , and  $\text{A}^8$  are independently selected at each occurrence from the group:  $\text{NR}^{13}$ ,  $\text{NR}^{13}\text{R}^{14}$ , S, SH, S(Pg), OH, and a bond to  $\text{L}_n$ ;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group:  $\text{C}_1\text{-C}_{10}$  alkyl substituted with 0-3  $\text{R}^{17}$ , aryl substituted with 0-3  $\text{R}^{17}$ ,  $\text{C}_3\text{-10}$  cycloalkyl substituted with 0-3  $\text{R}^{17}$ , and a 5-10 membered heterocyclic ring system containing

1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

5 R<sup>13</sup> and R<sup>14</sup> are each independently selected from the group: a bond to L<sub>n</sub>, hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>, and  
10 an electron, provided that when one of R<sup>13</sup> or R<sup>14</sup> is an electron, then the other is also an electron;

alternatively, R<sup>13</sup> and R<sup>14</sup> combine to form =C(R<sup>20</sup>)(R<sup>21</sup>);

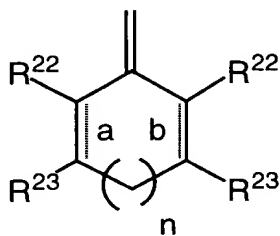
15 R<sup>17</sup> is independently selected at each occurrence from the group: a bond to L<sub>n</sub>, =O, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CH<sub>2</sub>OR<sup>18</sup>, -OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OR<sup>18</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>C(=O)R<sup>18</sup>, -NR<sup>19</sup>C(=O)OR<sup>18a</sup>, -NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>,  
20 -NR<sup>19</sup>SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>18a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>18a</sup>, -S(=O)R<sup>18a</sup>, -SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -N(R<sup>18</sup>)<sub>2</sub>, -NHC(=S)NHR<sup>18</sup>, =NOR<sup>18</sup>, -C(=O)NHN(R<sup>18</sup>)R<sup>18a</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H, and 2-(1-morpholino)ethoxy;

25 R<sup>18</sup>, R<sup>18a</sup>, and R<sup>19</sup> are independently selected at each occurrence from the group: a bond to L<sub>n</sub>, H, and C<sub>1</sub>-C<sub>6</sub> alkyl;

30 R<sup>20</sup> and R<sup>21</sup> are independently selected from the group: H, C<sub>1</sub>-C<sub>5</sub> alkyl, -CO<sub>2</sub>R<sup>25</sup>, C<sub>2</sub>-C<sub>5</sub> 1-alkene substituted with 0-3 R<sup>23</sup>, C<sub>2</sub>-C<sub>5</sub> 1-alkyne substituted with 0-3 R<sup>23</sup>, aryl substituted with 0-3 R<sup>23</sup>, and unsaturated 5-10 membered heterocyclic ring system containing 1-4

heteroatoms independently selected from N, S, and O  
and substituted with 0-3 R<sup>23</sup>;

alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the  
5 divalent carbon radical to which they are attached  
form:



10 R<sup>22</sup> and R<sup>23</sup> are independently selected from the group: H,  
and R<sup>24</sup>;

alternatively, R<sup>22</sup>, R<sup>23</sup> taken together form a fused  
aromatic or a 5-10 membered heterocyclic ring system  
15 containing 1-4 heteroatoms independently selected  
from N, S, and O;

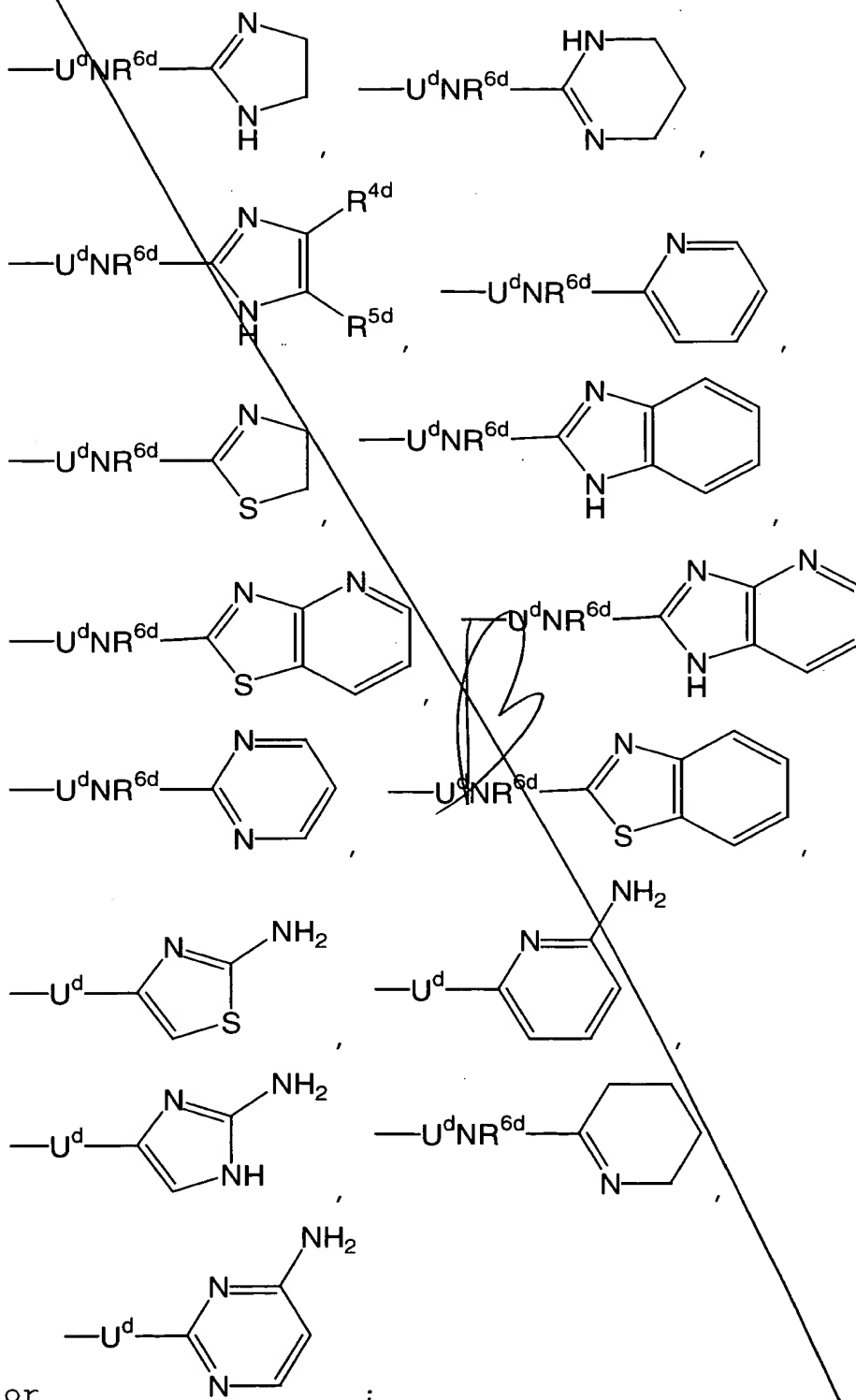
R<sup>24</sup> is independently selected at each occurrence from the  
group: -CO<sub>2</sub>R<sup>25</sup>, -C(=O)N(R<sup>25</sup>)<sub>2</sub>, -CH<sub>2</sub>OR<sup>25</sup>, -OC(=O)R<sup>25</sup>,  
-OR<sup>25</sup>, -SO<sub>3</sub>H, -N(R<sup>25</sup>)<sub>2</sub>, and -OCH<sub>2</sub>CO<sub>2</sub>H; and,

20 R<sup>25</sup> is independently selected at each occurrence from the  
group: H and C<sub>1</sub>-C<sub>3</sub> alkyl.

4. A compound according to Claim 3, wherein:  
25



R<sup>1de</sup> is selected from:



wherein the above heterocycles are optionally substituted with 0-2 substituents selected from the group: NH<sub>2</sub>,

halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkyl, and C<sub>3</sub>-C<sub>7</sub> cycloalkyl;

U<sup>d</sup> is -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>t</sub> Q<sup>d d</sup> (CH<sub>2</sub>)<sub>m</sub>- or -C(=O)(CH<sub>2</sub>)<sub>n</sub>-1-,

5 wherein one of the methylene groups is optionally substituted with R<sup>7d</sup>;

R<sup>7d</sup> is selected from: C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl),  
10 heteroaryl, and heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl);

R<sup>10d</sup> is selected from: H, R<sup>1de</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, halogen, CO<sub>2</sub>R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>,  
15 C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

20 R<sup>10de</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, halogen, CO<sub>2</sub>R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>,  
25 C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

W<sup>d</sup> is -C(=O)-N(R<sup>13d</sup>)-;

30 X<sup>d</sup> is -CH(R<sup>14d</sup>)-CH(R<sup>15d</sup>)-;

R<sup>13d</sup> is H or CH<sub>3</sub>;

R<sup>14d</sup> is selected from:

H, C<sub>1</sub>-C<sub>10</sub> alkyl, aryl, or heteroaryl, wherein said aryl or heteroaryl groups are optionally substituted with 0-3 substituents selected from the group consisting of: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, aryl, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

R<sup>15d</sup> is H or R<sup>16d</sup>;

Y<sup>d</sup> is -COR<sup>19d</sup>;

R<sup>19d</sup> is selected from:

hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, methylcarbonyloxymethoxy-, ethylcarbonyloxymethoxy-, t-butylcarbonyloxymethoxy-, cyclohexylcarbonyloxymethoxy-, 1-(methylcarbonyloxy)ethoxy-, 1-(ethylcarbonyloxy)ethoxy-, 1-(t-butylcarbonyloxy)ethoxy-, 1-(cyclohexylcarbonyloxy)ethoxy-, i-propyloxy carbonyloxymethoxy-, t-butyloxy carbonyloxymethoxy-, 1-(i-propyloxy carbonyloxy)ethoxy-, 1-(cyclohexyloxy carbonyloxy)ethoxy-, 1-(t-butyloxy carbonyloxy)ethoxy-, dimethylaminoethoxy-, diethylaminoethoxy-, (5-methyl-1,3-dioxacyclopenten-2-on-4-yl)methoxy-, (5-(t-butyl)-1,3-dioxacyclopenten-2-on-4-yl)methoxy-, (1,3-dioxo-5-phenyl-cyclopenten-2-on-4-yl)methoxy-, and 1-(2-(2-methoxypropyl) carbonyloxy)ethoxy-;

R<sup>20d</sup> is H or CH<sub>3</sub>;

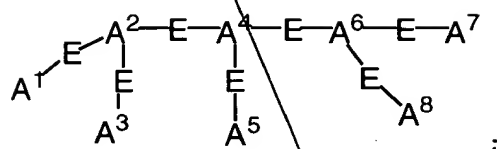
$m^d$  is 0 or 1;

$n^d$  is 1-4;

$t^d$  is 0 or 1;

5

$C_h$  is



10

$A^1$  is selected from the group: OH, and a bond to  $L_n$ ;

$A^2$ ,  $A^4$ , and  $A^6$  are each N;

15

$A^3$ ,  $A^5$ , and  $A^8$  are each OH;

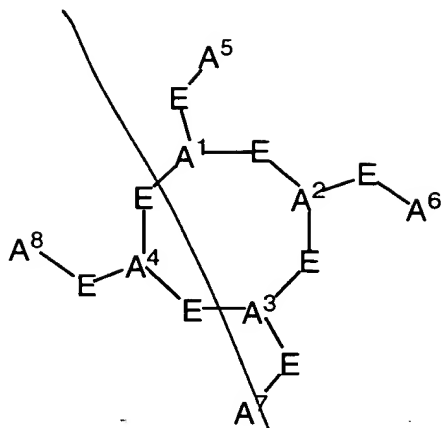
$A^7$  is a bond to  $L_n$  or NH-bond to  $L_n$ ;

E is a  $C_2$  alkyl substituted with 0-1  $R^{17}$ ;

20

$R^{17}$  is =O;

alternatively,  $C_h$  is



$A^1$  is selected from the group: OH and a bond to  $L_n$ ;

5

$A^2$ ,  $A^3$  and  $A^4$  are each N;

$A^5$ ,  $A^6$  and  $A^8$  are each OH;

10  $A^7$  is a bond to  $L_n$ ;

E is a  $C_2$  alkyl substituted with 0-1  $R^{17}$ ;

$R^{17}$  is =O;

15 alternatively,  $C_h$  is  $A^1-E-A^2$ ;

$A^1$  is  $NH_2$  or  $N=C(R^{20})(R^{21})$ ;

E is a bond;

20

$A^2$  is  $NHR^{13}$ ;

$R^{13}$  is a heterocycle substituted with  $R^{17}$ , the heterocycle being selected from pyridine and pyrimidine;

25

R<sup>17</sup> is selected from a bond to L<sub>n</sub>, C(=O)NHR<sup>18</sup> and  
C(=O)R<sup>18</sup>;

R<sup>18</sup> is a bond to L<sub>n</sub>;

5

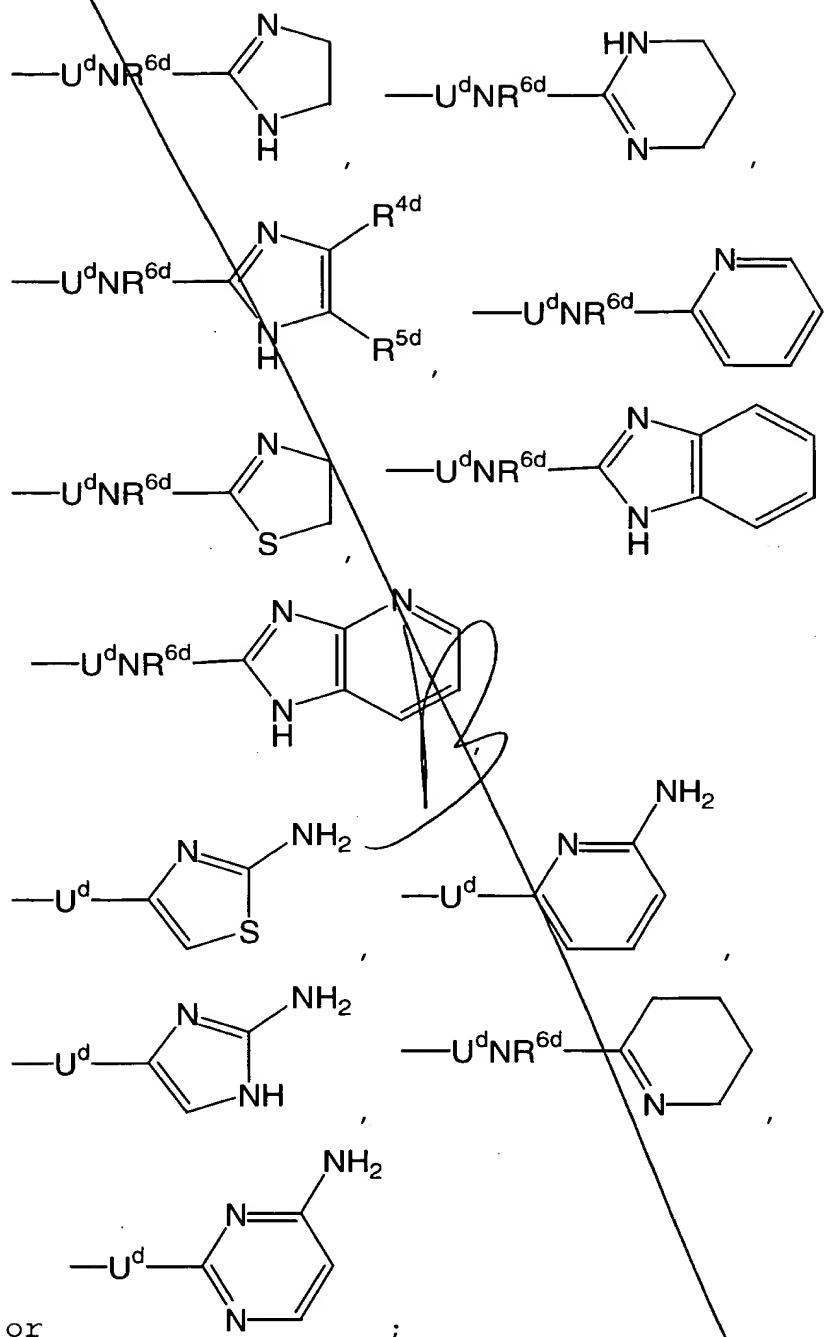
R<sup>24</sup> is selected from the group: -CO<sub>2</sub>R<sup>25</sup>, -OR<sup>25</sup>, -SO<sub>3</sub>H, and  
-N(R<sup>25</sup>)<sub>2</sub>; and

10

R<sup>25</sup> is independently selected at each occurrence from the  
group: hydrogen and methyl.

5. A compound according to Claim 4, wherein:

R<sup>1de</sup> is selected from:



wherein the above heterocycles are optionally substituted with 0-2 substituents selected from the group: NH<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkyl, and C<sub>3</sub>-C<sub>7</sub> cycloalkyl.

15

6. A compound according to Claim 2, wherein the compound is selected from the group:

5 2-(((4-(4-(((3-(2-(2-(3-((6-((1-aza-2-(2-sulfophenyl)vinyl)amino)(3-pyridyl))carbonylamino)propoxy)-ethoxy)ethoxy)propyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)-3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid;

15 2-(2-aza-2-((5-(N-(1,3-bis(3-(2-(2-(3-(((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)ethyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)propoxy)-ethoxy)ethoxy)propyl)carbamoyl)propyl)carbamoyl)(2-pyridyl))amino)vinyl)benzenesulfonic acid;

20 2-((6-((1-aza-2-(sulfophenyl)vinyl)amino)(3-pyridyl))carbonylamino)-4-(N-(3-(2-(2-(3-(((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-ethyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)-amino)propoxy)-ethoxy)ethoxy)propyl)carbamoyl)butanoic acid;

30 3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-2-(((4-(4-(((3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-cyclododecyl)-acetylamino)propoxy)ethoxy)ethoxy)propyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)amino)propanoic acid;

35 2-(6-((6-((1-aza-2-(2-sulfophenyl)vinyl)-amino)(3-pyridyl))carbonylamino)hexanoylamino)-3-((1-(3-



(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-propanoic acid;

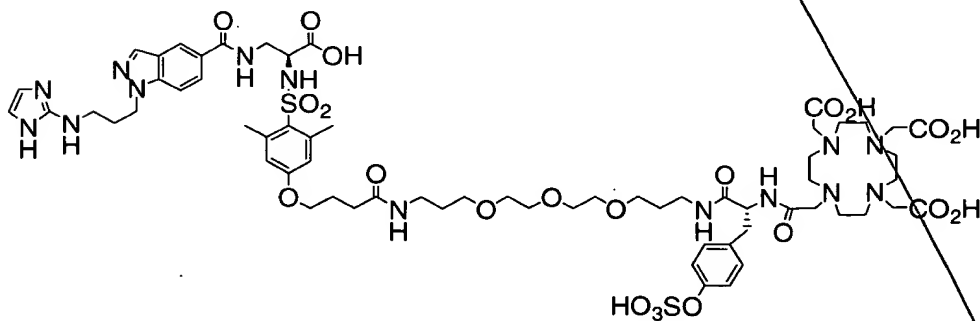
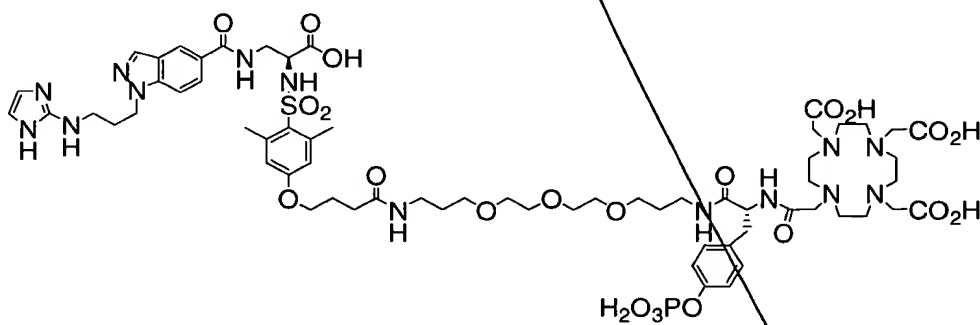
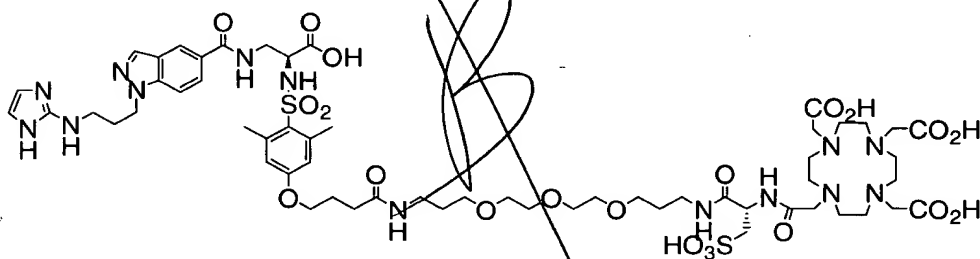
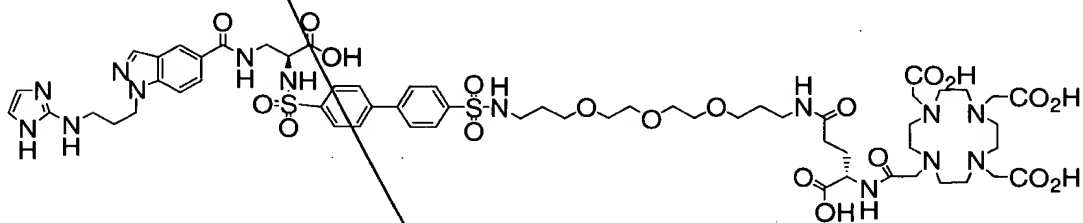
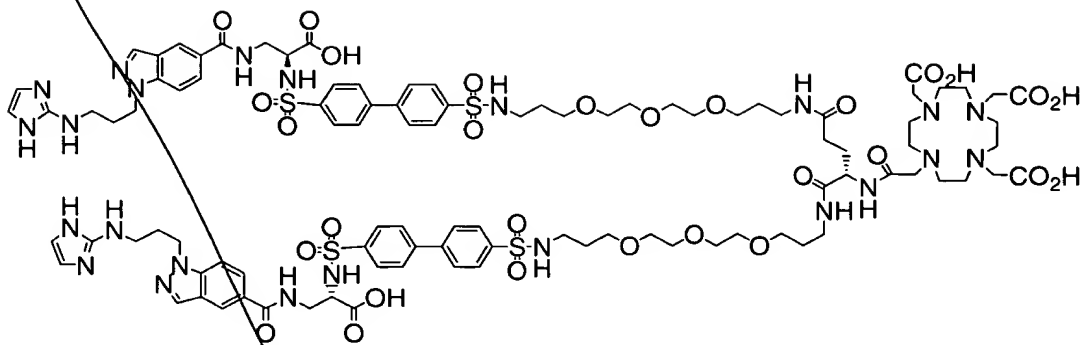
2-((6-((1-aza-2-(2-sulfophenyl)vinyl)-amino)(3-pyridyl))carbonylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid;

[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono)methyl]-benzenesulfonic acid]-Glu(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid);

[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono)methyl]-benzenesulfonic acid]-Glu-bis-[Glu(2-(6-Aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)];

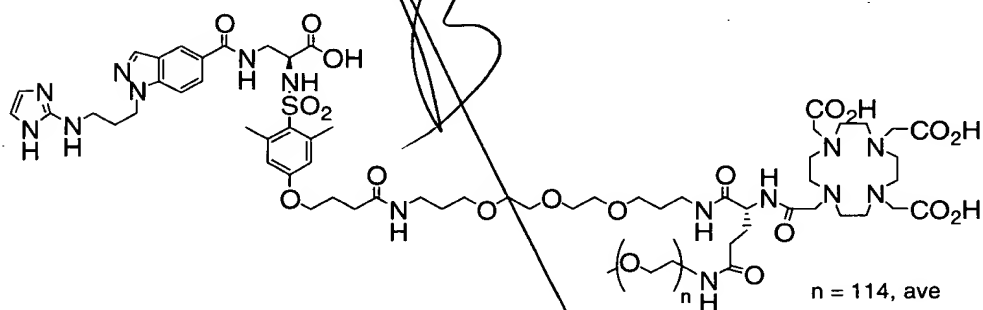
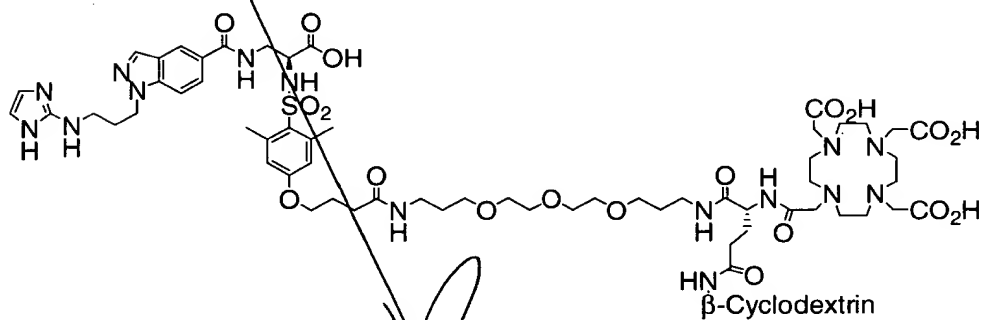
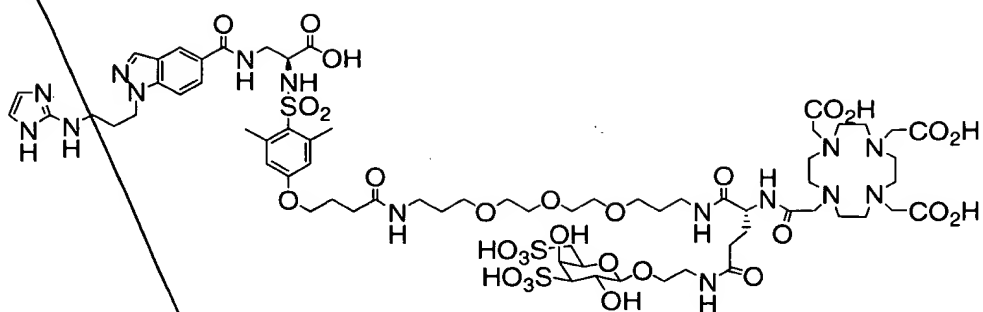
2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-{2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid};

2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu{2-(6-Aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid}{2-(6-Aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid};

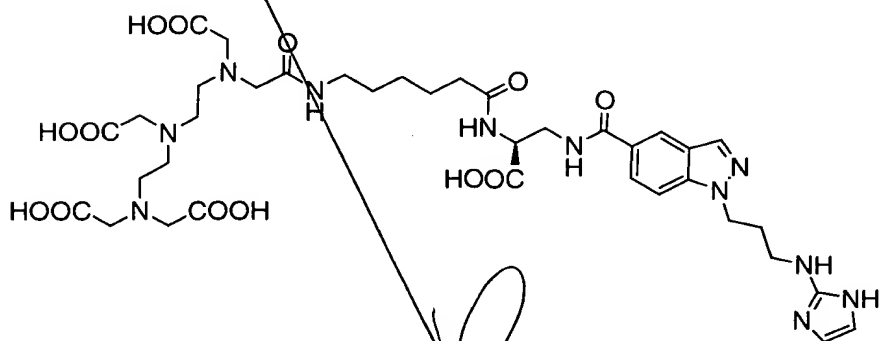
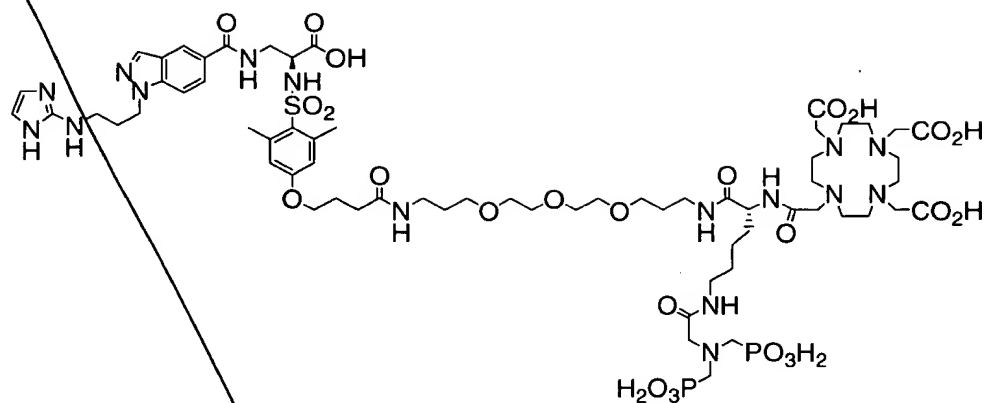


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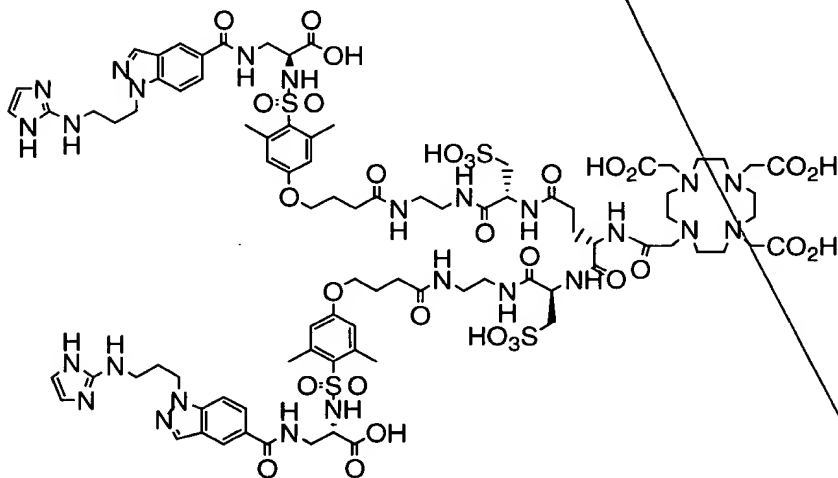
10



2-(((4-(3-(N-(3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-  
 tris(carboxymethyl)cyclododecylacetyl amino)-6-  
 aminohexanoyl amino)propoxy)ethoxy)ethoxy)propyl)-  
 carbamoyl)propoxy)-2,6-dimethylphenyl)-  
 sulfonyl)amino)-3-((1-(3-(imidazol-2-  
 yl amino)propyl)(1H-indazol-5-yl))carbonyl amino)-  
 propionic acid salt;



- 5 2-([4-(3-{N-[2-((2R)-3-Sulfo-2-{2-[1,4,7,10-tetraaza-  
4,7,10-tris(carboxymethyl)cyclododecyl]acetylamino}-  
propyl)ethyl]carbamoyl}propoxy)-2,6-dimethylphenyl]-  
sulfonyl)amino) (2S)-3-({1-[3-(imidazol-2-  
ylamino)propyl] (1H-indazol-5-  
yl)}carbonylamino)propanoic Acid;
- 10



2-[(4-[4-([2-((2R)-3-Sulfo-2-{2-[1,4,7,10-tetraaza-  
4,7,10-tris(carboxymethyl)cyclododecyl]-  
acetylamino}propyl)ethyl)amino)sulfonyl)phenyl]phenyl  
sulfonyl)amino](2S)-3-([1-[3-(imidazol-2-  
ylamino)propyl](1H-indazol-5-  
yl)]carbonylamino)propanoic Acid;

(4S)-4-(N-{1-[N-(2-{4-[4-([1-(1S)-1-carboxy-2-([1-[3-(2-  
pyridylamino)propyl](1H-indazol-5-  
yl)]carbonylamino)ethyl)amino)sulfonyl]-3,5-  
dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-  
carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-  
4,7,10-  
tris(carboxymethyl)cyclododecyl]acetylamino}butanoic  
acid;

(4S)-4-(N-{1-[N-(2-{4-[4-([1-(1S)-1-carboxy-2-([1-[3-  
(imidazol-2-ylamino)propyl](1H-indazol-5-  
yl)]carbonylamino)ethyl)amino)sulfonyl]-3,5-  
dimethylphenoxy]butanoylamino}ethyl)carbamoyl]-3-  
carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-  
4,7,10-  
tris(carboxymethyl)cyclododecyl]acetylamino}butanoic  
acid;

(4S)-4-{N-[(1S)-1-(N-{1,3-bis[N-(2-{4-[4-([1-(1S)-1-  
carboxy-2-([1-[3-(imidazol-2-ylamino)propyl](1H-  
indazol-5-yl)]carbonylamino)ethyl)amino)sulfonyl]-  
3,5-  
dimethylphenoxy]butanoylamino}ethyl)carbamoyl]propyl  
}carbamoyl)-3-carboxypropyl]carbamoyl)-4-(6-{2-  
[1,4,7,10-tetraaza-4,7,10-  
tris(carboxymethyl)cyclododecyl]acetylamino}  
hexanoylamino)butanoic acid;

(4S)-4-(N-{1-[N-(2-{4-[4-([1-(1S)-1-carboxy-2-([1-[3-  
(3,4,5,6-tetrahydropyrimidin-2-ylamino)propyl](1H-

indazol-5-yl)}carbonylamino)ethyl]amino)sulfonyl)-  
3,5-dimethylphenoxy]butanoylamino)ethyl)carbamoyl]-  
3-carboxy propyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-  
4,7,10-tris

5 (carboxymethyl)cyclododecyl]acetylamino}butanoic  
acid;

(4S)-4-(N-{1-[N-(2-{4-[4-(((1S)-1-carboxy-2-({1-methyl-  
3-[3-(2-3,4,5,6-tetrahydropyridylamino)propyl] (1H-  
10 indazol-6-yl)}carbonylamino)ethyl]amino)sulfonyl)-  
3,5-dimethylphenoxy]butanoylamino)ethyl)carbamoyl]-  
3-carboxypropyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-  
4,7,10-  
tris(carboxymethyl)cyclododecyl]acetylamino}butanoic  
15 acid;

(4S)-4-(N-{(1S)-1-[N-(2-{4-[4-(((1S)-1-carboxy-2-({1-[2-  
(2-3,4,5,6-tetrahydropyridylamino)ethyl] (1H-  
indazol-5-yl)}carbonylamino)ethyl]amino)sulfonyl)-  
20 3,5-dimethylphenoxy]butanoylamino)ethyl)carbamoyl]-  
3-carboxy propyl}carbamoyl)-4-{2-[1,4,7,10-tetraaza-  
4,7,10-tris  
(carboxymethyl)cyclododecyl]acetylamino}butanoic  
acid;

25 (2S)-2-{{(2,6-dimethyl-4-{3-[N-(2-{2-[1,4,7,10-tetraaza-  
4,7,10-tris(carboxymethyl)cyclododecyl]acetyl-  
amino)ethyl)carbamoyl]propoxy}phenyl)sulfonyl]amino}  
-3-({2-[2-(2-3,4,5,6-  
30 tetrahydropyridylamino)ethyl](2-hydro-1H-indazol-5-  
yl)}carbonylamino)propanoic acid;

(4S)-4-{N-[(1S)-1-(N-{2-[(4-[4-(((1S)-1-carboxy-2-({1-  
[2-(2-3,4,5,6-tetrahydropyridylamino)ethyl] (1H-  
35 indazol-5-  
yl)}carbonylamino)ethyl]amino)sulfonyl]phenyl]  
phenyl)sulfonyl]amino]ethyl}carbamoyl)-3-

carboxypropyl] carbamoyl}-4-{2-[1,4,7,10-tetraaza-  
4,7,10-tris(carboxy-  
methyl)cyclododecyl]acetylamino}butanoic acid;

5 (4S)-4-{N-[(1S)-1-(N-{2-[(4-[4-[(1S)-1-carboxy-2-({1-  
[3-(3,4,5,6-tetrahydropyrimidin-2-ylamino)  
propyl](1H-indazol-5-  
yl))carbonylamino)ethyl]amino)sulfonyl]  
phenyl]phenyl)sulfonyl]amino}ethyl]carbamoyl}-3-

10 carboxy propyl]carbamoyl}-4-{2-[1,4,7,10-tetraaza-  
4,7,10-tris  
(carboxymethyl)cyclododecyl]acetylamino}butanoic  
acid;

15 (2S)-3-({3-[(imidazol-2-ylamino) methyl]-1-methyl(1H-  
indazol-6-yl))carbonylamino)-2-({[4-(4-[(2-{2-  
[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)  
cyclododecyl]acetylamino)ethyl]amino)sulfonyl]phenyl  
)phenyl]sulfonyl]amino}propanoic acid;

20 3-[(7-{3-[(6-[(1E)-1-aza-2-(2-  
sulfophenyl)vinyl]amino)}(3-  
pyridyl))carbonylamino]propoxy}-1-[3-(imidazol-2-  
ylamino)propyl](1H-indazol-5-yl))-  
25 carbonylamino](2S)-2-[(2,4,6-  
trimethylphenyl)sulfonyl]-amino}propanoic acid;  
and

30 3-[[1-[3-(imidazol-2-ylamino)propyl]-7-(3-{2-[1,4,7,10-  
tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl]-  
acetylamino}propoxy)(1H-indazol-5-  
yl)]carbonylamino}-2-[(2,4,6-  
trimethylphenyl)sulfonyl]amino}propanoic acid;

35 or a pharmaceutically acceptable salt form thereof.

7. A kit comprising a compound of Claim 2, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.
- 5 8. A kit according to Claim 7, wherein the kit further comprises one or more ancillary ligands and a reducing agent.
9. A kit according to Claim 8, wherein the ancillary  
10 ligands are tricine and TPPTS.
10. A kit according to Claim 8, wherein the reducing agent is tin(II).
- 15 11. A diagnostic or therapeutic metallopharmaceutical composition, comprising: a metal, a chelator capable of chelating the metal and a targeting moiety, wherein the targeting moiety is bound to the chelator, is an indazole nonpeptide and binds to a  
20 receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups between the targeting moiety and chelator.
12. A composition according to Claim 11, wherein the  
25 metallopharmaceutical is a diagnostic radiopharmaceutical, the metal is a radioisotope selected from the group:  $^{99m}\text{Tc}$ ,  $^{95}\text{Tc}$ ,  $^{111}\text{In}$ ,  $^{62}\text{Cu}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Ga}$ , and  $^{68}\text{Ga}$ , and the linking group is present between the targeting moiety and chelator.
- 30 13. A composition according to Claim 12, wherein the targeting moiety is an indazole and the receptor is  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$ .
- 35 14. A composition according to Claim 13, wherein the radioisotope is  $^{99m}\text{Tc}$  or  $^{95}\text{Tc}$ , the



radiopharmaceutical further comprises a first ancillary ligand and a second ancillary ligand capable of stabilizing the radiopharmaceutical.

5 15. A composition according to Claim 14, wherein the radioisotope is  $^{99m}\text{Tc}$ .

16. A composition according to Claim 15, wherein the radiopharmaceutical is selected from the group:

10

$^{99m}\text{Tc}$  (((4-(4-(((3-(2-(2-(3-((6-(diazenido)(3-pyridyl))carbonylamino)propoxy)-ethoxy)ethoxy)propyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)-3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid) (tricine) (TPPTS);

15

$^{99m}\text{Tc}$  (2-(2-((5-(N-(1,3-bis(3-(2-(2-(3-(((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)ethyl)amino)sulfonyl)-phenyl)phenyl)sulfonyl)amino)propoxy)-ethoxy)ethoxy)propyl)carbamoyl)propyl)carbamoyl)(2-pyridyl))2-diazenido) (tricine) (TPPTS);

20

25  $^{99m}\text{Tc}$  (2-((6-(diazenido)(3-pyridyl))carbonylamino)-4-(N-(3-(2-(2-(3-(((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-ethyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)-amino)propoxy)-ethoxy)ethoxy)propyl)carbamoyl)butanoic acid) (tricine) (TPPTS);

30

$^{99m}\text{Tc}$  (2-(6-((6-(diazenido)(3-pyridyl))carbonylamino)hexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-propanoic acid) (tricine) (TPPTS);

35

<sup>99m</sup>Tc (2-((6-(diazenido)(3-pyridyl))carbonylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid (tricine) (TPPTS);

5 <sup>99m</sup>Tc [2-[[[5-[carbonyl]-2-pyridinyl]diazenido]-Glu(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid))

10 (tricine) (TPPTS);

<sup>99m</sup>Tc ([2-[[[5-[carbonyl]-2-pyridinyl]diazenido]-Glu-bis-[Glu(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid))]

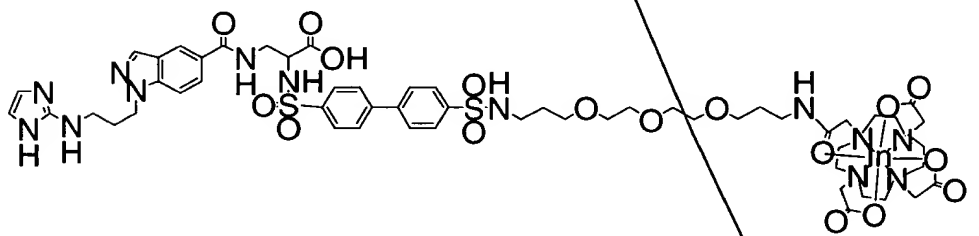
15 (tricine) (TPPTS);

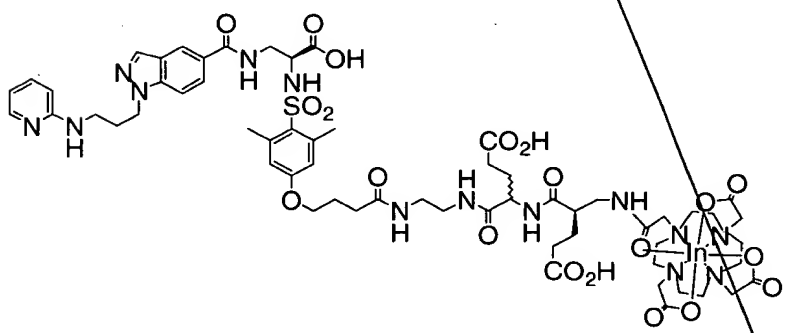
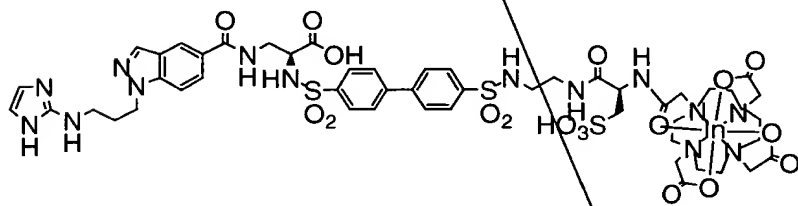
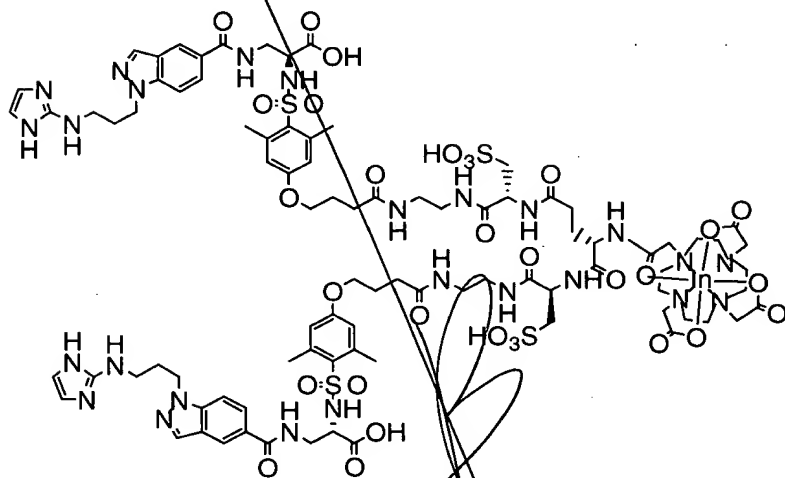
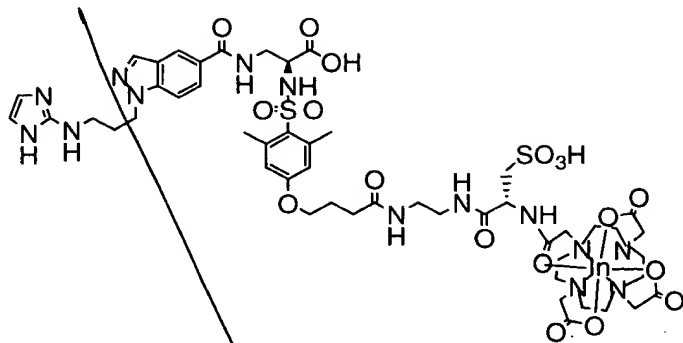
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17. A composition according to Claim 13, wherein the radioisotope is <sup>111</sup>In.

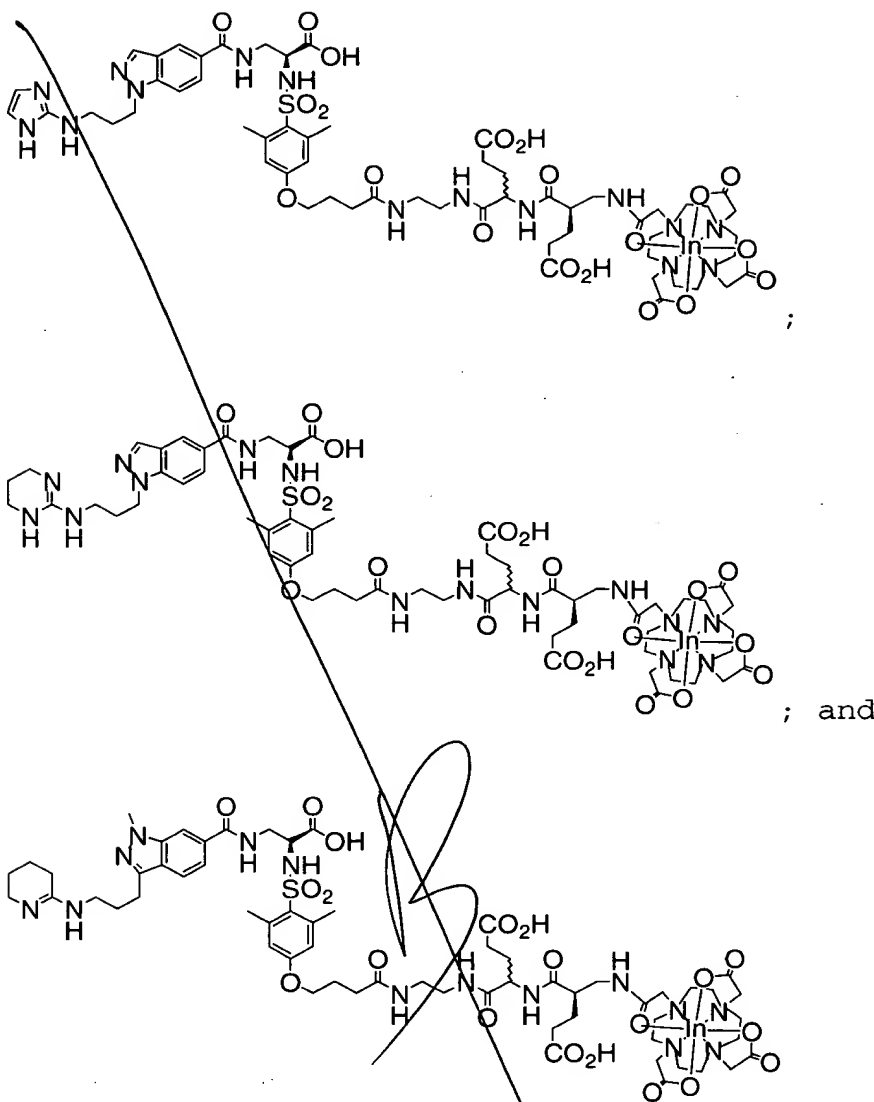
18. A composition according to Claim 17, wherein, the

25 radiopharmaceutical is selected from the group:





5



5

19. A composition according to Claim 11, wherein the metallopharmaceutical is a therapeutic
- 10 radiopharmaceutical, the metal is a radioisotope selected from the group:  $^{33}\text{P}$ ,  $^{125}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{153}\text{Sm}$ ,  $^{166}\text{Ho}$ ,  $^{177}\text{Lu}$ ,  $^{149}\text{Pm}$ ,  $^{90}\text{Y}$ ,  $^{212}\text{Bi}$ ,  $^{103}\text{Pd}$ ,  $^{109}\text{Pd}$ ,  $^{159}\text{Gd}$ ,  $^{140}\text{La}$ ,  $^{198}\text{Au}$ ,  $^{199}\text{Au}$ ,  $^{169}\text{Yb}$ ,  $^{175}\text{Yb}$ ,  $^{165}\text{Dy}$ ,  $^{166}\text{Dy}$ ,  $^{67}\text{Cu}$ ,  $^{105}\text{Rh}$ ,  $^{111}\text{Ag}$ , and  $^{192}\text{Ir}$ , the targeting moiety is an indazole nonpeptide and the
- 15 linking group is present between the targeting moiety and chelator.

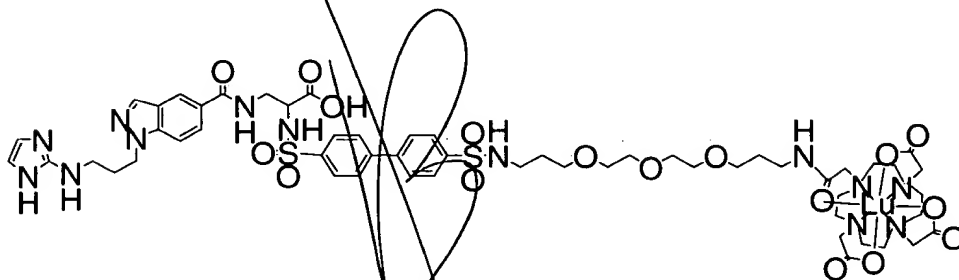
20. A composition according to Claim 19, wherein the targeting moiety is an indazole and the receptor is  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$ .

5 21. A composition according to Claim 20, wherein the radioisotope is  $^{153}\text{Sm}$ .

22. A composition according to Claim 20, wherein the radioisotope is  $^{177}\text{Lu}$ .

10

23. A composition according to Claim 22, wherein the radiopharmaceutical is

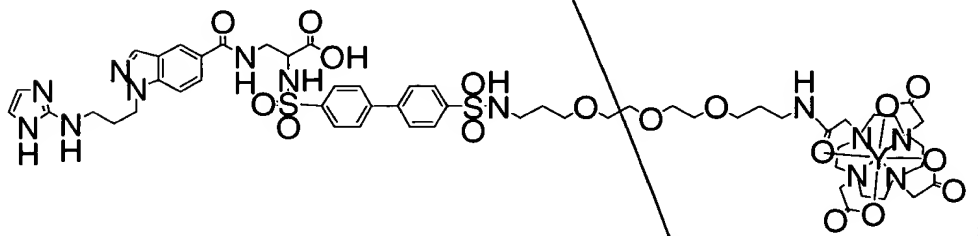


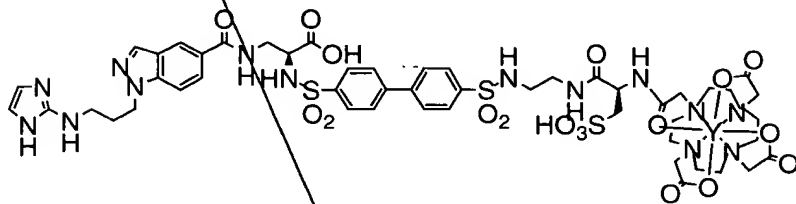
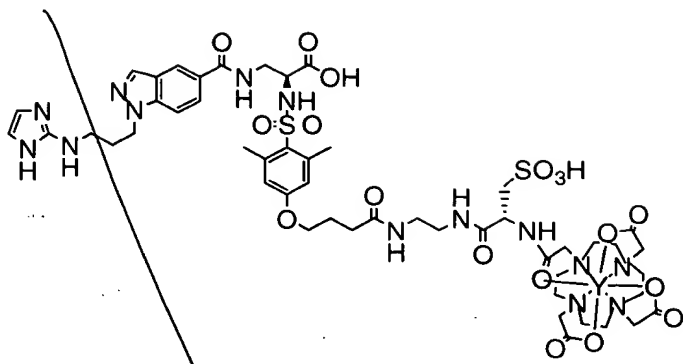
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24. A composition according to Claim 20, wherein the radioisotope is  $^{90}\text{Y}$ .

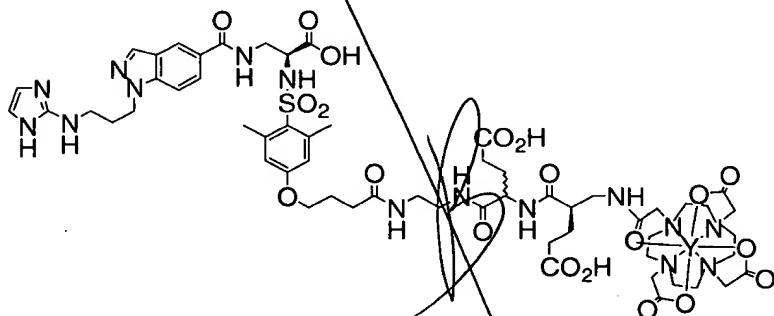
25. A composition according to Claim 24, wherein, the radiopharmaceutical is selected from the group:

20





; and



5

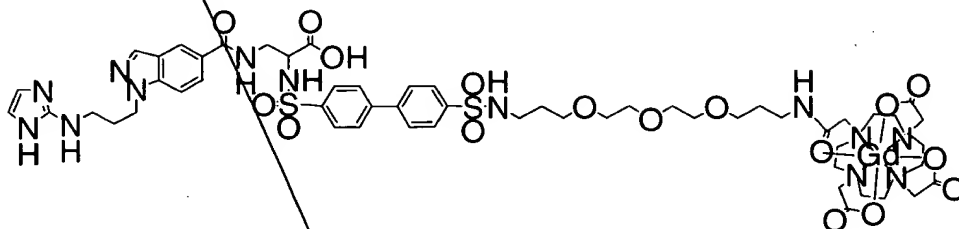
26. A composition according to Claim 11, wherein the  
 metallopharmaceutical is a MRI contrast agent, the  
 metal is a paramagnetic metal ion selected from the  
 group: Gd(III), Dy(III), Fe(III), and Mn(II), the  
 targeting moiety is an indazole nonpeptide and the  
 linking group is present between the targeting  
 moiety and chelator.

15

27. A composition according to Claim 26, wherein the  
 targeting moiety is an indazole and the receptor is  
 $\alpha_v\beta_3$  or  $\alpha_v\beta_5$ .

28. A composition according to Claim 27, wherein the metal ion is Gd(III).

29. A composition according to Claim 28, wherein the contrast agent is



30. A composition according to Claim 11, wherein the metallopharmaceutical is a X-ray contrast agent, the metal is selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, the targeting moiety comprises an indazole, the receptor is  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$ , and the linking group is present between the targeting moiety and chelator.

31. A method of treating rheumatoid arthritis in a patient comprising: administering a therapeutic radiopharmaceutical of Claim 19 capable of localizing in new angiogenic vasculature to a patient by injection or infusion.

32. A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical of Claim 19 by injection or infusion.

33. A method of treating restenosis in a patient comprising: administering to a patient, either systemically or locally, a therapeutic radiopharmaceutical of Claim 19 capable of

localizing in the restenotic area and delivering an effective dose of radiation.

34. A method of imaging therapeutic angiogenesis in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11 to a patient by injection or infusion; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.
35. A method of imaging atherosclerosis in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11 to a patient by injection or infusion; (2) imaging the area of the patient wherein the atherosclerosis is located.
36. A method of imaging restenosis in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11 to a patient by injection or infusion; (2) imaging the area of the patient wherein the restenosis is located.
37. A method of imaging cardiac ischemia in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11 to a patient by injection or infusion; (2) imaging the area of the myocardium wherein the ischemic region is located.
38. A method of imaging myocardial reperfusion injury in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11 to a patient by injection or infusion; (2) imaging the

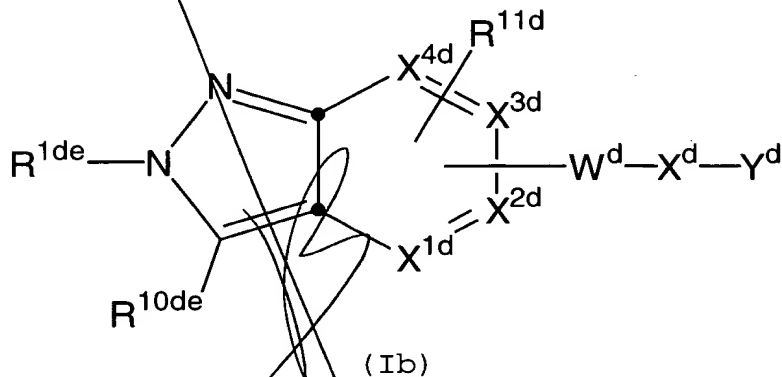
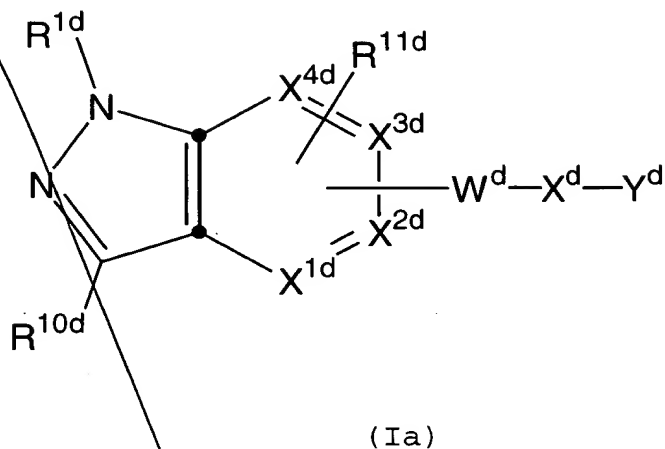


area of myocardium wherein the reperfusion injury is located.

39. A method of imaging cancer in a patient comprising:  
5 (1) administering a diagnostic radiopharmaceutical of Claim 12 to a patient by injection or infusion;  
(2) imaging the patient using planar or SPECT gamma scintigraphy, or positron emission tomography.
- 10 40. A method of imaging cancer in a patient comprising:  
(1) administering a MRI contrast agent of Claim 27;  
and (2) imaging the patient using magnetic resonance imaging.
- 15 41. A method of imaging cancer in a patient comprising:  
(1) administering a X-ray contrast agent of Claim 30; and (2) imaging the patient using X-ray computed tomography.
- 20 42. A compound, comprising: a targeting moiety and a surfactant, wherein the targeting moiety is bound to the surfactant, is an indazole nonpeptide, and binds to a receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups  
25 between the targeting moiety and surfactant.
43. A compound according to Claim 42, wherein the linking group is present between the targeting moiety and surfactant.
- 30 44. A compound according to Claim 43, wherein the receptor is the integrin  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$  and the compound is of the formula:

35 (Q)<sub>d</sub>-L<sub>n</sub>-S<sub>f</sub>

wherein, Q is a independently a compound of Formulae (Ia) or (Ib):



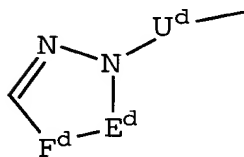
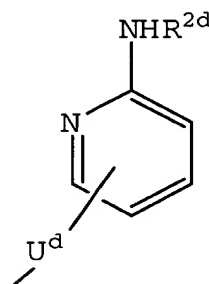
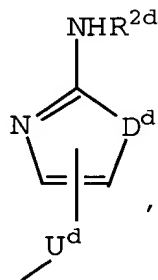
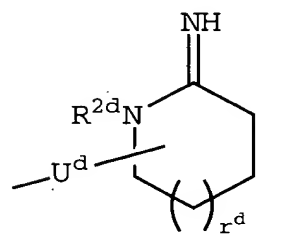
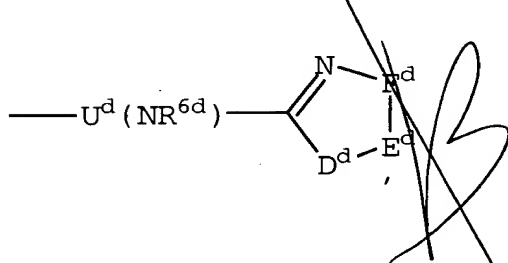
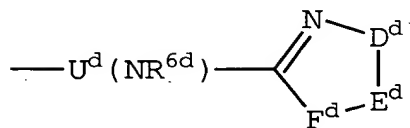
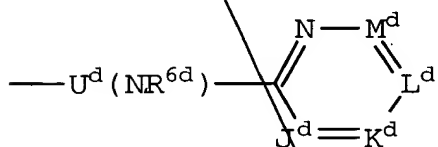
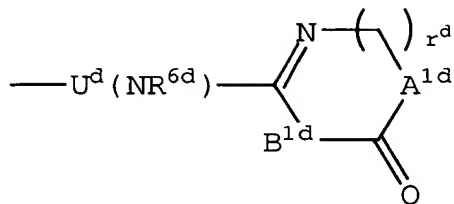
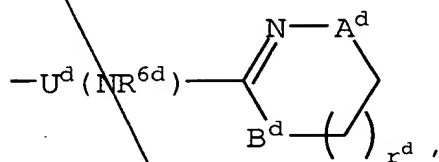
including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof wherein:

- 15  $X^{1d}$  is N, CH, C- $W^d$ - $X^d$ - $Y^d$ , or C- $L_n$ ;  
 $X^{2d}$  is N, CH, or C- $W^d$ - $X^d$ - $Y^d$ ;  
 $X^{3d}$  is N,  $CR^{11d}$ , or C- $W^d$ - $X^d$ - $Y^d$ ;  
 $X^{4d}$  is N or  $CR^{11d}$ ;

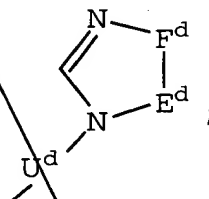
- 20 provided that when  $R^{1d}$  is  $R^{1de}$  then one of  $X^{1d}$  and  $X^{2d}$  is C- $W^d$ - $X^d$ - $Y^d$ , and when  $R^{10d}$  is  $R^{1de}$  then  $X^{3d}$  is C- $W^d$ - $X^d$ - $Y^d$ ;

5 ~~R<sup>1d</sup> is selected from: R<sup>1de</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with  
0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with  
0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted  
with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl  
substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl  
substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2  
R<sup>11d</sup> or 0-1 R<sup>21d</sup>;~~

$R^{1de}$  is selected from:



or



A<sup>d</sup> and B<sup>d</sup> are independently -CH<sub>2</sub>-, -O-, -N(R<sup>2d</sup>)-, or -C(=O)-;

A<sup>1d</sup> and B<sup>1d</sup> are independently -CH<sub>2</sub>- or -N(R<sup>3d</sup>)-;

D<sup>d</sup> is -N(R<sup>2d</sup>)-, -O-, -S-, -C(=O)- or -SO<sub>2</sub>-;

5

E<sup>d</sup>-F<sup>d</sup> is -C(R<sup>4d</sup>)=C(R<sup>5d</sup>)-, -N=C(R<sup>4d</sup>)-, -C(R<sup>4d</sup>)=N-, or -  
C(R<sup>4d</sup>)<sub>2</sub>C(R<sup>5d</sup>)<sub>2</sub>-;

J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> are independently selected from:

10 -C(R<sup>4d</sup>)-, -C(R<sup>5d</sup>)- and -N-, provided that at least  
one of J<sup>d</sup>, K<sup>d</sup>, L<sup>d</sup> and M<sup>d</sup> is not -N-;

R<sup>2d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, (C<sub>1</sub>-C<sub>6</sub>  
alkyl)carbonyl, (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl; (C<sub>1</sub>-C<sub>6</sub>  
15 alkyl)aminocarbonyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
alkyl)carbonyl, heteroarylcabonyl,  
aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl-,  
arylcabonyl, C<sub>1</sub>-C<sub>6</sub> alkylsulfonyl, arylsulfonyl,  
20 aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)sulfonyl, heteroarylsulfonyl,  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)sulfonyl, aryloxycarbonyl, and  
aryl(C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl, wherein said aryl groups  
are substituted with 0-2 substituents selected from  
the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy,  
25 halo, CF<sub>3</sub>, and nitro;

R<sup>3d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

30

R<sup>4d</sup> and R<sup>5d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>4</sub>  
alkoxy, NR<sup>2d</sup>R<sup>3d</sup>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl,  
C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub>  
cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, (C<sub>1</sub>-C<sub>6</sub>

alkyl)carbonyl, (C<sub>1</sub>-C<sub>6</sub> alkoxy)carbonyl, arylcarbonyl,  
or

alternatively, when substituents on adjacent atoms, R<sup>4d</sup>

5 and R<sup>5d</sup> can be taken together with the carbon atoms  
to which they are attached to form a 5-7 membered  
carbocyclic or 5-7 membered heterocyclic aromatic or  
non-aromatic ring system, said carbocyclic or  
heterocyclic ring being optionally substituted with  
10 0-2 groups selected from: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy,  
halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

U<sup>d</sup> is selected from:

- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>-,
- 15 - (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(CR<sup>7d</sup>=CR<sup>8d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C≡C)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>t<sup>d</sup></sub>Q(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>O(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- 20 - (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>C(=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>(C=O)N(R<sup>6d</sup>)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-,
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>N(R<sup>6d</sup>)(C=O)(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-, and
- (CH<sub>2</sub>)<sub>n<sup>d</sup></sub>S(O)<sub>p<sup>d</sup></sub>(CH<sub>2</sub>)<sub>m<sup>d</sup></sub>-;

25 wherein one or more of the methylene groups in U<sup>d</sup> is  
optionally substituted with R<sup>7d</sup>;

Q<sup>d</sup> is selected from 1,2-cycloalkylene, 1,2-phenylene,  
1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-  
30 pyridinylene, 2,4-pyridinylene, and 3,4-  
pyridazinylene;

R<sup>6d</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkyl, or benzyl;

R<sup>7d</sup> and R<sup>8d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and heteroaryl(C<sub>0</sub>-C<sub>6</sub> alkyl)-;

R<sup>10d</sup> is selected from: H, R<sup>1de</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

R<sup>10de</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, N(R<sup>6d</sup>)<sub>2</sub>, halogen, NO<sub>2</sub>, CN, CF<sub>3</sub>, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, -SO<sub>2</sub>R<sup>17d</sup>, -SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>6</sub> alkenyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl substituted with 0-1 R<sup>15d</sup> or 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>15d</sup> or 0-2 R<sup>11d</sup> or 0-1 R<sup>21d</sup>;

R<sup>11d</sup> is selected from H, halogen, CF<sub>3</sub>, CN, NO<sub>2</sub>, hydroxy, NR<sup>2d</sup>R<sup>3d</sup>, C<sub>1</sub>-C<sub>4</sub> alkyl substituted with 0-1 R<sup>21d</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy substituted with 0-1 R<sup>21d</sup>, aryl substituted with 0-1 R<sup>21d</sup>, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- substituted with 0-1 R<sup>21d</sup>, (C<sub>1</sub>-C<sub>4</sub> alkoxy)carbonyl substituted with 0-1 R<sup>21d</sup>, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl substituted with 0-1 R<sup>21d</sup>,

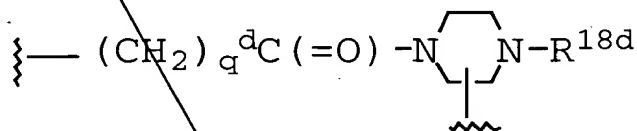
C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl substituted with 0-1 R<sup>21d</sup>, and  
 C<sub>1</sub>-C<sub>4</sub> alkylaminosulfonyl substituted with 0-1 R<sup>21d</sup>;

W<sup>d</sup> is selected from:

- 5    -(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>C(=O)N(R<sup>13d</sup>)-, and  
       -C(=O)-N(R<sup>13d</sup>)-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>-;

X<sup>d</sup> is -C(R<sup>12d</sup>)(R<sup>14d</sup>)-C(R<sup>12d</sup>)(R<sup>15d</sup>)-; or

- 10    alternatively, W<sup>d</sup> and X<sup>d</sup> can be taken together to be



- 15    R<sup>12d</sup> is selected from H, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub>  
       alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
       C<sub>4</sub>-C<sub>10</sub> cycloalkylalkyl, (C<sub>1</sub>-C<sub>4</sub> alkyl)carbonyl, aryl,  
       and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

- 20    R<sup>13d</sup> is selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub>  
       cycloalkylmethyl, and aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

- 25    R<sup>14d</sup> is selected from:  
       H, C<sub>1</sub>-C<sub>6</sub> alkylthio(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub>  
       alkylthioalkyl)-, aryl(C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl)-, C<sub>1</sub>-C<sub>10</sub>  
       alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl, C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, C<sub>2</sub>-C<sub>10</sub>  
       alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-C<sub>10</sub>  
       cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
       alkyl)-, aryl, heteroaryl, CO<sub>2</sub>R<sup>17d</sup>, C(=O)R<sup>17d</sup>, and  
       CONR<sup>17d</sup>R<sup>20d</sup>, provided that any of the above alkyl,  
       cycloalkyl, aryl or heteroaryl groups may be  
       unsubstituted or substituted independently with 0-1  
       R<sup>16d</sup> or 0-2 R<sup>11d</sup>;
- 30

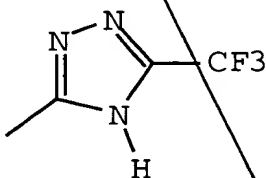
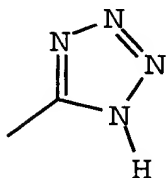


R<sup>15d</sup> is selected from:

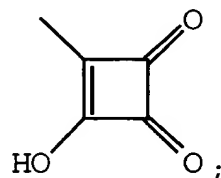
H, R<sup>16d</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxyalkyl,  
 C<sub>1</sub>-C<sub>10</sub> alkylaminoalkyl, C<sub>1</sub>-C<sub>10</sub> dialkylaminoalkyl,  
 5 (C<sub>1</sub>-C<sub>10</sub> alkyl)carbonyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)carbonyl,  
 C<sub>1</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>3</sub>-  
 C<sub>10</sub> cycloalkylalkyl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-,  
 heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, aryl, heteroaryl, CO<sub>2</sub>R<sup>17d</sup>,  
 C(=O)R<sup>17d</sup>, CONR<sup>17d</sup>R<sup>20d</sup>, SO<sub>2</sub>R<sup>17d</sup>, and SO<sub>2</sub>NR<sup>17d</sup>R<sup>20d</sup>,  
 10 provided that any of the above alkyl, cycloalkyl,  
 aryl or heteroaryl groups may be unsubstituted or  
 substituted independently with 0-2 R<sup>11d</sup>;

Y<sup>d</sup> is selected from:

15 -COR<sup>19d</sup>, -SO<sub>3</sub>H, -PO<sub>3</sub>H, tetrazolyl, -CONHNHSO<sub>2</sub>CF<sub>3</sub>, -  
 CONHSO<sub>2</sub>R<sup>17d</sup>, -CONHSO<sub>2</sub>NHR<sup>17d</sup>, -NHCOCF<sub>3</sub>, -NHCONHSO<sub>2</sub>R<sup>17d</sup>,  
 -NHSO<sub>2</sub>R<sup>17d</sup>, -OPO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H, -PO<sub>3</sub>H<sub>2</sub>, -SO<sub>3</sub>H, -  
 SO<sub>2</sub>NHCOR<sup>17d</sup>, -SO<sub>2</sub>NHCO<sub>2</sub>R<sup>17d</sup>,



, and



R<sup>16d</sup> is selected from:

-N(R<sup>20d</sup>)-C(=O)-O-R<sup>17d</sup>,  
 25 -N(R<sup>20d</sup>)-C(=O)-R<sup>17d</sup>,  
 -N(R<sup>20d</sup>)-C(=O)-NH-R<sup>17d</sup>,  
 -N(R<sup>20d</sup>)SO<sub>2</sub>-R<sup>17d</sup>, and  
 -N(R<sup>20d</sup>)SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

30 R<sup>17d</sup> is selected from:

C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with a bond to  
 L<sub>n</sub>, C<sub>3</sub>-C<sub>11</sub> cycloalkyl optionally substituted with a  
 bond to L<sub>n</sub>, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally substituted  
 with a bond to L<sub>n</sub>, (C<sub>1</sub>-C<sub>6</sub> alkyl)aryl optionally  
 5 substituted with a bond to L<sub>n</sub>, heteroaryl(C<sub>1</sub>-C<sub>6</sub>  
 alkyl)- optionally substituted with a bond to L<sub>n</sub>,  
 (C<sub>1</sub>-C<sub>6</sub> alkyl)heteroaryl optionally substituted with a  
 bond to L<sub>n</sub>, biaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)- optionally  
 substituted with a bond to L<sub>n</sub>, heteroaryl optionally  
 10 substituted with a bond to L<sub>n</sub>, aryl optionally  
 substituted with a bond to L<sub>n</sub>, biaryl optionally  
 substituted with a bond to L<sub>n</sub>, and a bond to L<sub>n</sub>,  
 wherein said aryl, biaryl or heteroaryl groups are  
 also optionally substituted with 0-3 substituents  
 15 selected from the group: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy,  
 aryl, heteroaryl, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

R<sup>18d</sup> is selected from:

-H,  
 20 -C(=O)-O-R<sup>17d</sup>,  
 -C(=O)-R<sup>17d</sup>,  
 -C(=O)-NH-R<sup>17d</sup>,  
 -SO<sub>2</sub>-R<sup>17d</sup>, and  
 -SO<sub>2</sub>-NR<sup>20d</sup>R<sup>17d</sup>;

25

R<sup>19d</sup> is selected from: hydroxy, C<sub>1</sub>-C<sub>10</sub> alkyloxy,  
 C<sub>3</sub>-C<sub>11</sub> cycloalkyloxy, aryloxy, aryl(C<sub>1</sub>-C<sub>6</sub> alkoxy)-,  
 C<sub>3</sub>-C<sub>10</sub> alkylcarbonyloxyalkyloxy, C<sub>3</sub>-C<sub>10</sub>  
 alkoxycarbonyloxyalkyloxy,  
 30 C<sub>2</sub>-C<sub>10</sub> alkoxycarbonylalkyloxy,  
 C<sub>5</sub>-C<sub>10</sub> cycloalkylcarbonyloxyalkyloxy,  
 C<sub>5</sub>-C<sub>10</sub> cycloalkoxycarbonyloxyalkyloxy,  
 C<sub>5</sub>-C<sub>10</sub> cycloalkoxycarbonylalkyloxy,  
 C<sub>7</sub>-C<sub>11</sub> aryloxycarbonylalkyloxy,

~~C<sub>8</sub>-C<sub>12</sub> aryloxy-carbonyloxyalkyloxy,  
 C<sub>8</sub>-C<sub>12</sub> arylcarbonyloxyalkyloxy,  
 C<sub>5</sub>-C<sub>10</sub> alkoxyalkylcarbonyloxyalkyloxy,  
 C<sub>5</sub>-C<sub>10</sub> (5-alkyl-1,3-dioxo-cyclopenten-2-one-  
 5 yl)methyloxy, C<sub>10</sub>-C<sub>14</sub> (5-aryl-1,3-dioxo-cyclopenten-  
 2-one-yl)methyloxy, and  
 (R<sup>11d</sup>) (R<sup>12d</sup>)N-(C<sub>1</sub>-C<sub>10</sub> alkoxy)-;~~

10 R<sup>20d</sup> is selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
 C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and  
 heteroaryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

R<sup>21d</sup> is selected from: COOH and NR<sup>6d</sup><sub>2</sub>;

m<sup>d</sup> is 0-4;

15 n<sup>d</sup> is 0-4;

t<sup>d</sup> is 0-4;

p<sup>d</sup> is 0-2;

q<sup>d</sup> is 0-2; and

r<sup>d</sup> is 0-2;

20

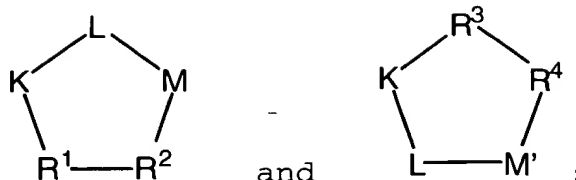
with the following provisos:

(1) t<sup>d</sup>, n<sup>d</sup>, m<sup>d</sup> and q<sup>d</sup> are chosen such that the number of  
 atoms connecting R<sup>1d</sup> and Y<sup>d</sup> is in the range of 10-14;  
 and

25 (2) n<sup>d</sup> and m<sup>d</sup> are chosen such that the value of n<sup>d</sup> plus  
 m<sup>d</sup> is greater than one unless U<sup>d</sup> is  
 $-(CH_2)_t Q^d (CH_2)_m^-$ ;

or Q is a peptide selected from the group:

30



R<sup>1</sup> is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L<sub>n</sub>;

5 R<sup>2</sup> is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L<sub>n</sub>;

10 R<sup>3</sup> is D-valine;

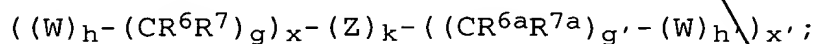
R<sup>4</sup> is D-tyrosine substituted on the hydroxy group with a bond to L<sub>n</sub>;

15 provided that one of R<sup>1</sup> and R<sup>2</sup> in each Q is substituted with a bond to L<sub>n</sub>, and further provided that when R<sup>2</sup> is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

20 provided that at least one Q is a compound of Formula Ia or Ib;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25 L<sub>n</sub> is a linking group having the formula:



W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, NR<sup>8</sup>C(=O), C(=O)N  
 30 R<sup>8</sup>, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, SO<sub>2</sub>NH, (OCH<sub>2</sub>CH<sub>2</sub>)<sub>20-200</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>20-200</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>20-200</sub>, (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>20-200</sub>, and (aa)<sub>t</sub>;

aa is independently at each occurrence an amino acid;

5 Z is selected from the group: aryl substituted with 0-3  $R^{10}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-3  $R^{10}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{10}$ ;

10  $R^6$ ,  $R^{6a}$ ,  $R^7$ ,  $R^{7a}$ , and  $R^8$  are independently selected at each occurrence from the group: H, =O, COOH,  $SO_3H$ ,  $PO_3H$ ,  $C_1-C_5$  alkyl substituted with 0-3  $R^{10}$ , aryl substituted with 0-3  $R^{10}$ , benzyl substituted with 0-3  $R^{10}$ , and  $C_1-C_5$  alkoxy substituted with 0-3  $R^{10}$ ,  
15  $NHC(=O)R^{11}$ ,  $C(=O)NHR^{11}$ ,  $NHC(=O)NHR^{11}$ ,  $NHR^{11}$ ,  $R^{11}$ , and a bond to  $S_f$ ;

$R^{10}$  is independently selected at each occurrence from the group: a bond to  $S_f$ ,  $COOR^{11}$ ,  $C(=O)NHR^{11}$ ,  $NHC(=O)R^{11}$ ,  
20 OH,  $NHR^{11}$ ,  $SO_3H$ ,  $PO_3H$ ,  $-OPO_3H_2$ ,  $-OSO_3H$ , aryl substituted with 0-3  $R^{11}$ ,  $C_{1-5}$  alkyl substituted with 0-1  $R^{12}$ ,  $C_{1-5}$  alkoxy substituted with 0-1  $R^{12}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{11}$ ;

25  $R^{11}$  is independently selected at each occurrence from the group: H, alkyl substituted with 0-1  $R^{12}$ , aryl substituted with 0-1  $R^{12}$ , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1  $R^{12}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-1  $R^{12}$ , and a bond to  $S_f$ ;

30

R<sup>12</sup> is a bond to S<sub>f</sub>;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

5 h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

10 x' is selected from 0, 1, 2, 3, 4, and 5;

S<sub>f</sub> is a surfactant which is a lipid or a compound of the

formula:  $A^9-E^1-A^{10}$ ;

15 A<sup>9</sup> is selected from the group: OH and OR<sup>27</sup>;

A<sup>10</sup> is OR<sup>27</sup>;

R<sup>27</sup> is C(=O)C<sub>1-20</sub> alkyl;

20

E<sup>1</sup> is C<sub>1-10</sub> alkylene substituted with 1-3 R<sup>28</sup>;

R<sup>28</sup> is independently selected at each occurrence from the  
group: R<sup>30</sup>, -PO<sub>3</sub>H-R<sup>30</sup>, =O, -CO<sub>2</sub>R<sup>29</sup>, -C(=O)R<sup>29</sup>,

25 -C(=O)N(R<sup>29</sup>)<sub>2</sub>, -CH<sub>2</sub>OR<sup>29</sup>, -OR<sup>29</sup>, -N(R<sup>29</sup>)<sub>2</sub>, C<sub>1</sub>-C<sub>5</sub>  
alkyl, and C<sub>2</sub>-C<sub>4</sub> alkenyl;

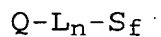
R<sup>29</sup> is independently selected at each occurrence from the  
group: R<sup>30</sup>, H, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, benzyl, and  
30 trifluoromethyl;

R<sup>30</sup> is a bond to L<sub>n</sub>;

and a pharmaceutically acceptable salt thereof.

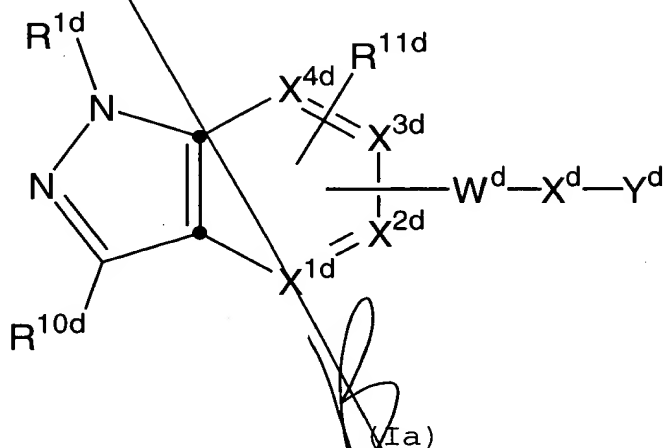
45. A compound according to Claim 44, wherein the compound is of the formula:

5

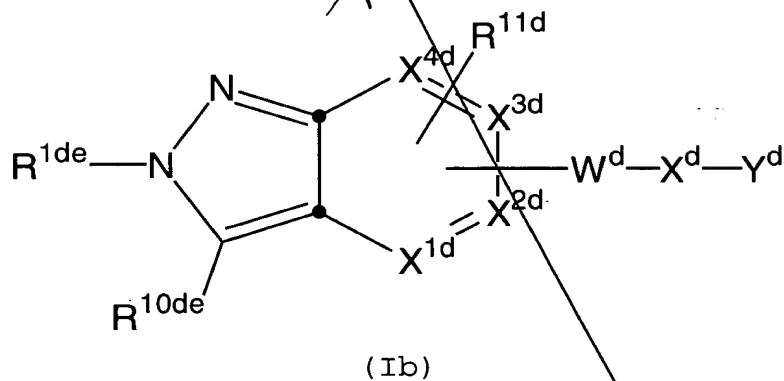


wherein: Q is a compound of Formula (Ia) or (Ib):

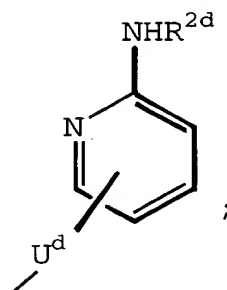
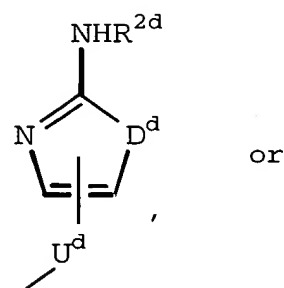
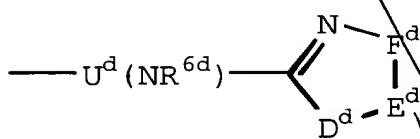
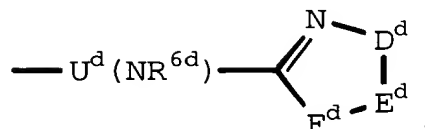
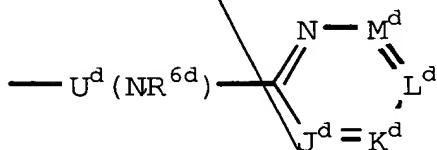
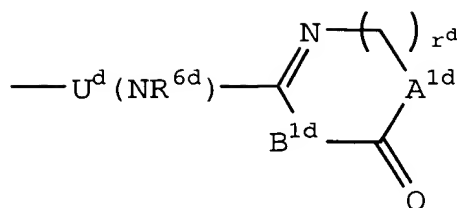
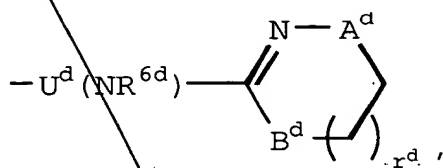
10



15



R<sup>1de</sup> is selected from:



5 A<sup>d</sup> and B<sup>d</sup> are independently -CH<sub>2</sub>-, -O-, -N(R<sup>2d</sup>)-, or -C(=O)-;

A<sup>1d</sup> and B<sup>1d</sup> are independently -CH<sub>2</sub>- or -N(R<sup>3d</sup>)-;

D<sup>d</sup> is -N(R<sup>2d</sup>)-, -O-, -S-, -C(=O)- or -SO<sub>2</sub>-;



$E^{d,F}$  is  $-C(R^{4d})=C(R^{5d})-$ ,  $-N=C(R^{4d})-$ ,  $-C(R^{4d})=N-$ , or  $-C(R^{4d})_2C(R^{5d})_2-$ ;

$J^d$ ,  $K^d$ ,  $L^d$  and  $M^d$  are independently selected from:

5  $-C(R^{4d})-$ ,  $-C(R^{5d})-$  and  $-N-$ , provided that at least one of  $J^d$ ,  $K^d$ ,  $L^d$  and  $M^d$  is not  $-N-$ ;

$R^{2d}$  is selected from: H,  $C_1-C_6$  alkyl,  $(C_1-C_6$   
alkyl)carbonyl,  $(C_1-C_6$  alkoxy)carbonyl,  $C_1-C_6$   
10 alkylaminocarbonyl,  $C_3-C_6$  alkenyl,  $C_3-C_7$  cycloalkyl,  
 $C_4-C_{11}$  cycloalkylalkyl, aryl, heteroaryl( $C_1-C_6$   
alkyl)carbonyl, heteroarylcarbonyl, aryl( $C_1-C_6$   
alkyl)-,  $(C_1-C_6$  alkyl)carbonyl, arylcarbonyl,  
alkylsulfonyl, arylsulfonyl, aryl( $C_1-C_6$   
15 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl( $C_1-C_6$   
alkyl)sulfonyl, aryloxy carbonyl, and aryl( $C_1-C_6$   
alkoxy)carbonyl, wherein said aryl groups are  
substituted with 0-2 substituents selected from the  
group:  $C_1-C_4$  alkyl,  $C_1-C_4$  alkoxy, halo,  $CF_3$ , and  
20 nitro;

$R^{3d}$  is selected from: H,  $C_1-C_6$  alkyl,  $C_3-C_7$  cycloalkyl,  
 $C_4-C_{11}$  cycloalkylalkyl, aryl, aryl( $C_1-C_6$  alkyl)-, and  
heteroaryl( $C_1-C_6$  alkyl)-;

25  $R^{4d}$  and  $R^{5d}$  are independently selected from: H,  $C_1-C_4$   
alkoxy,  $NR^{2d}R^{3d}$ , halogen,  $NO_2$ , CN,  $CF_3$ ,  $C_1-C_6$  alkyl,  
 $C_3-C_6$  alkenyl,  $C_3-C_7$  cycloalkyl,  $C_4-C_{11}$   
cycloalkylalkyl, aryl, aryl( $C_1-C_6$  alkyl)-,  $C_2-C_7$   
30 alkylcarbonyl, and arylcarbonyl or

alternatively, when substituents on adjacent atoms,  $R^{4d}$   
and  $R^{5d}$  can be taken together with the carbon atoms

to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with  
 5 0-2 groups selected from: C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halo, cyano, amino, CF<sub>3</sub>, and NO<sub>2</sub>;

U<sup>d</sup> is selected from:

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> (CR<sup>7d</sup>=CR<sup>8d</sup>) (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

10 -(CH<sub>2</sub>)<sub>t</sub><sup>d</sup> Q<sup>d</sup> (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> O(CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> N(R<sup>6d</sup>) (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-,

-(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> C(=O) (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-, and

15 -(CH<sub>2</sub>)<sub>n</sub><sup>d</sup> S(O)<sub>p</sub><sup>d</sup> (CH<sub>2</sub>)<sub>m</sub><sup>d</sup>-;

wherein one or more of the methylene groups in U<sup>d</sup> is optionally substituted with R<sup>7d</sup>;

20 Q<sup>d</sup> is selected from 1,2-phenylene, 1,3-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, and 2,4-pyridinylene;

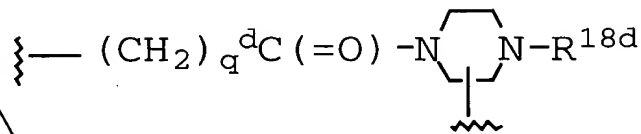
R<sup>6d</sup> is selected from: H, C<sub>1</sub>-C<sub>4</sub> alkyl, and benzyl;

25 R<sup>7d</sup> and R<sup>8d</sup> are independently selected from: H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>4</sub>-C<sub>11</sub> cycloalkylalkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub> alkyl)-, and heteroaryl(C<sub>0</sub>-C<sub>6</sub> alkyl)-;

30 W<sup>d</sup> is -C(=O)-N(R<sup>13d</sup>)-(C(R<sup>12d</sup>)<sub>2</sub>)<sub>q</sub><sup>d</sup>-;

$X^d$  is  $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$ ;

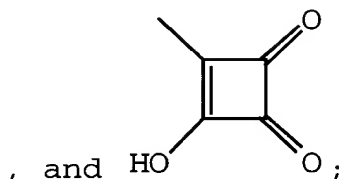
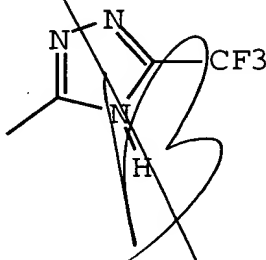
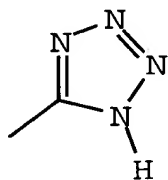
alternatively,  $W^d$  and  $X^d$  can be taken together to be



$R^{12d}$  is H or  $C_1-C_6$  alkyl;

$Y^d$  is selected from:

$-COR^{19d}$ ,  $-SO_3H$ ,



$Z$  is selected from the group: aryl substituted with 0-1  $R^{10}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-1  $R^{10}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1  $R^{10}$ ;

$R^6$ ,  $R^{6a}$ ,  $R^7$ ,  $R^{7a}$ , and  $R^8$  are independently selected at each occurrence from the group: H, =O, COOH,  $SO_3H$ ,  $C_1-C_5$  alkyl substituted with 0-1  $R^{10}$ , aryl substituted with 0-1  $R^{10}$ , benzyl substituted with 0-1  $R^{10}$ , and  $C_1-C_5$  alkoxy substituted with 0-1  $R^{10}$ ,  $NHC(=O)R^{11}$ ,  $C(=O)NHR^{11}$ ,  $NHC(=O)NHR^{11}$ ,  $NHR^{11}$ ,  $R^{11}$ , and a bond to  $S_f$ ;

k is 0 or 1;

S<sub>f</sub> is a surfactant which is a lipid or a compound of the

formula:  $A^9-E^1-A^{10}$ ;

A<sup>9</sup> is OR<sup>27</sup>;

A<sup>10</sup> is OR<sup>27</sup>;

R<sup>27</sup> is C(=O)C<sub>1-15</sub> alkyl;

E<sup>1</sup> is C<sub>1-4</sub> alkylene substituted with 1-3 R<sup>28</sup>;

R<sup>28</sup> is independently selected at each occurrence from the group: R<sup>30</sup>, -PO<sub>3</sub>H-R<sup>30</sup>, =O, -CO<sub>2</sub>R<sup>29</sup>, -C(=O)R<sup>29</sup>, -CH<sub>2</sub>OR<sup>29</sup>, -OR<sup>29</sup>, and C<sub>1</sub>-C<sub>5</sub> alkyl;

R<sup>29</sup> is independently selected at each occurrence from the group: R<sup>30</sup>, H, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, and benzyl;

R<sup>30</sup> is a bond to L<sub>n</sub>;

and a pharmaceutically acceptable salt thereof.

46. A compound according to Claim 45, wherein the present invention provides a compound selected from the group:

DPPE-2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid-dodecanoate conjugate;

~~$\omega$ -amino-PEG<sub>3400</sub>-2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid; and~~

5  ~~$\omega$ -amino-PEG<sub>3400</sub>-Glu-(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)-propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)<sub>2</sub>.~~

- 10 47. An ultrasound contrast agent composition, comprising:
- (a) a compound of Claim 44, comprising: an indazole that binds to the integrin  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$  a surfactant and a linking group between the indazole and the surfactant;
- 15 (b) a parenterally acceptable carrier; and,
- (c) an echogenic gas.

20 48. An ultrasound contrast agent composition of Claim 47, further comprising: 1,2-dipalmitoyl-sn-glycero-3-phosphatidic acid, 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine, and N-(methoxypolyethylene glycol 5000 carbamoyl)-1,2-dipalmitoyl-sn-glycero-3-phosphatidylethanolamine.

25 49. An ultrasound contrast agent composition of Claim 48, wherein the echogenic gas is a C<sub>2-5</sub> perfluorocarbon.

30 50. A method of imaging cancer in a patient comprising:

(1) administering, by injection or infusion, a ultrasound contrast agent composition of Claim 44 to a patient; and (2) imaging the patient using sonography.

51. A method of imaging therapeutic angiogenesis in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of Claim 42 to a patient; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.
52. A method of imaging atherosclerosis in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of Claim 42 to a patient; (2) imaging the area of the patient wherein the atherosclerosis is located.
53. A method of imaging restenosis in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of Claim 42 to a patient; (2) imaging the area of the patient wherein the restenosis is located.
54. A method of imaging cardiac ischemia in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of Claim 42 to a patient; (2) imaging the area of the myocardium wherein the ischemic region is located.
55. A method of imaging myocardial reperfusion injury in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of Claim 42 to a patient; (2) imaging the area of myocardium wherein the reperfusion injury is located.
56. A therapeutic radiopharmaceutical composition, comprising:  
(a) a therapeutic radiopharmaceutical of Claim 19;  
and,

(b) a parenterally acceptable carrier.

57. A diagnostic pharmaceutical composition, comprising:  
(a) a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11; and,  
(b) a parenterally acceptable carrier.

58. A kit for treating cancer, comprising a compound of Claim 1, or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

59. A kit according to claim 58 wherein said kit comprises a plurality of separate containers, wherein at least one of said containers contains a compound of Claim 1, or a pharmaceutically acceptable salt thereof, and at least another of said containers contains one or more agents selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

60. A kit according to Claim 58, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine,

vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio Stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

61. A kit according to Claim 58, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminogluthethimide, amsacrine, proglumide, elliptinium acetate, ketanserine, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, and lisuride.

62. A kit according to Claim 58 wherein the chemotherapeutic agent is selected from the group consisting of oxymetholone, tamoxifen, progesterone, mepitiostane, epitio Stanol, and formestane.

63. A kit according to Claim 58 wherein the chemotherapeutic agent is selected from the group consisting of interferon-alpha, interferon-2 alpha,



interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

5

64. A kit according to Claim 58, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

10

15

65. A therapeutic metallopharmaceutical composition according to claim 11, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, further comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

Sub 20  
B2

25

66. A therapeutic metallopharmaceutical composition according to claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminogluthethimide, amsacrine, proglumide,

30

35

elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol,

Sub B2  
5 tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

10  
15 67. A therapeutic metallopharmaceutical composition according to claim 65, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamide, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

20  
25 68. A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical of Claim 19 or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

30 69. A method of treating cancer according to claim 68, wherein the administration is by injection or infusion.

35 70. A method according to claim 68 wherein administering the therapeutic radiopharmaceutical and agent is concurrent.

71. A method according to claim 68 wherein administering the therapeutic radiopharmaceutical and agent is sequential.
- 5 72. A method according to claim 68 wherein the cancer is selected from the group consisting of carcinomas of the lung, breast, ovary, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, prostate, thyroid, squamous cell carcinomas, adenocarcinomas, small cell carcinomas, melanomas, gliomas, and neuroblastomas.
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73. A method according to claim 68 wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftotox, interleukin-2, and leutinizing hormone releasing factor.
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74. A method according to claim 68 wherein the radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamide, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.
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75. A process for the preparation of diagnostic or therapeutic metallopharmaceutical composition, said process comprising generating a macrostructure from a plurality of molecular components wherein the plurality of components includes a targeting moiety and a chelator, wherein the targeting moiety is a indazole nonpeptide, which is bound to the chelator, and binds to a receptor that is upregulated during angiogenesis and the compound has 0-1 linking groups between the targeting moiety and chelator.
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add  
B<sup>3</sup>